

# WEST Search History

DATE: Wednesday, July 10, 2002

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DB=USPT,PGPB,JPAB,EPAB,DWPI; PLUR=YES; OP=OR

L12	L11 and @ad<19960523	7	L12
L11	L9 and (class adj II)	79	L11
L10	L9 and (class II)	92	L10
L9	L8 and (MHC)	92	L9
L8	((CD80 or B7.1) same(ICAM\$2 or CD54 or CD50 or CD102)) and (CD4 or CD4+)	107	L8
L7	(CD80 or B7.1) same(ICAM\$2 or CD54 or CD50 or CD102)	152	L7
L6	(CD80 or B7.1) and (ICAM\$2 or CD54 or CD50 or CD102)	254	L6
L5	L4 and (ICAM\$2 or CD54 or CD50 or CD102)	5	L5
L4	L3 and ((CD80 or B7.1))	5	L4
L3	L2 and CD4\$2	60	L3
L2	(webb)[IN] OR (wingvist)[IN] or(karlsson ) [in] or (Jackson) [in] or (peterson)[in]	33315	L2
L1	(webb)[IN] OR (wingvist)[IN]	5841	L1

END OF SEARCH HISTORY

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NEWS 4 Feb 01 DKILIT now produced by FIZ Karlsruhe and has a new update frequency  
NEWS 5 Feb 19 Access via Tymnet and SprintNet Eliminated Effective 3/31/02  
NEWS 6 Mar 08 Gene Names now available in BIOSIS  
NEWS 7 Mar 22 TOXLIT no longer available  
NEWS 8 Mar 22 TRCTHERMO no longer available  
NEWS 9 Mar 28 US Provisional Priorities searched with P in CA/CAplus and USPATFULL  
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NEWS 17 Apr 22 BIOSIS Gene Names now available in TOXCENTER  
NEWS 18 Apr 22 Federal Research in Progress (FEDRIP) now available  
NEWS 19 Jun 03 New e-mail delivery for search results now available  
NEWS 20 Jun 10 MEDLINE Reload  
NEWS 21 Jun 10 PCTFULL has been reloaded  
NEWS 22 Jul 02 FOREGE no longer contains STANDARDS file segment

NEWS EXPRESS February 1 CURRENT WINDOWS VERSION IS V6.0d,  
CURRENT MACINTOSH VERSION IS V6.0a(ENG) AND V6.0Ja(JP),  
AND CURRENT DISCOVER FILE IS DATED 05 FEBRUARY 2002  
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\* \* \* \* \* STN Columbus \* \* \* \* \*

FILE 'HOME' ENTERED AT 11:52:47 ON 10 JUL 2002

=> file medline caplus embase biosis  
COST IN U.S. DOLLARS SINCE FILE TOTAL  
FULL ESTIMATED COST ENTRY SESSION  
0.21 0.21

FILE 'MEDLINE' ENTERED AT 11:53:01 ON 10 JUL 2002

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FILE 'BIOSIS' ENTERED AT 11:53:01 ON 10 JUL 2002  
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=> s webb S?/au or Wingvist O?/au or karlsson L?/au or Jackson M?/au or Peterson P?/au  
L1 14884 WEBB S?/AU OR WINGVIST O?/AU OR KARLSSON L?/AU OR JACKSON M?/AU  
OR PETERSON P?/AU

=>

=> s l1 and cd4?  
L2 198 L1 AND CD4?

=> s l2 not cd40  
L3 185 L2 NOT CD40

=>

=> s l3 and (CD80 or B7.1)  
L4 13 L3 AND (CD80 OR B7.1)

=> dup rem 14  
PROCESSING COMPLETED FOR L4  
L5 6 DUP REM L4 (7 DUPLICATES REMOVED)

=> dis l5 1-6 ibib abs

L5 ANSWER 1 OF 6 MEDLINE DUPLICATE 1  
ACCESSION NUMBER: 2001296822 MEDLINE  
DOCUMENT NUMBER: 21270387 PubMed ID: 11376339  
TITLE: A key role for ICAM-1 in generating effector cells  
mediating inflammatory responses.  
AUTHOR: Camacho S A; Heath W R; Carbone F R; Sarvetnick N; LeBon A;  
Karlsson L; Peterson P A; Webb S

R  
CORPORATE SOURCE: Department of Immunology, IMM4, The Scripps Research Institute, 10550 North Torrey Pines Road, La Jolla, CA 92037, USA.  
CONTRACT NUMBER: AI39664 (NIAID)  
CA25803 (NCI)  
CA41993 (NCI)  
SOURCE: Nat Immunol, (2001 Jun) 2 (6) 523-9.  
Journal code: 100941354. ISSN: 1529-2908.  
PUB. COUNTRY: United States  
LANGUAGE: English  
FILE SEGMENT: Priority Journals  
ENTRY MONTH: 200106  
ENTRY DATE: Entered STN: 20010625  
Last Updated on STN: 20010625  
Entered Medline: 20010621

AB We investigated how the accessory molecule interactions encountered during T cell priming influence T cell-mediated destruction of insulin-producing beta cells and lead to type 1 diabetes. T cell receptor (TCR)-transgenic CD4+ T cells were primed under controlled conditions *in vitro* before being adoptively transferred into transgenic recipients expressing membrane ovalbumin under the control of the rat insulin promoter (RIP-mOVA). During priming, antigen-presenting cell expression of B7-1 without intracellular adhesion molecule 1 (ICAM-1) led to the generation of effector cells that migrated to the pancreata of RIP-mOVA recipients but did not cause diabetes. In contrast, when T cells were primed with APCs expressing both B7-1 and ICAM-1, pronounced destruction of beta cells and a rapid onset of diabetes were observed. Pathogenicity was associated with T cell production of the macrophage-attracting chemokines CCL3 and CCL4. Thus, interactions of lymphocyte function-associated antigen 1 with ICAM-1 during priming induce both qualitative and quantitative alterations in T effector function and induce potentially autodestructive responses.

L5 ANSWER 2 OF 6 CAPLUS COPYRIGHT 2002 ACS  
ACCESSION NUMBER: 2001:419849 CAPLUS  
DOCUMENT NUMBER: 136:100954  
TITLE: Vaccination with glutamic acid decarboxylase plasmid DNA protects mice from spontaneous autoimmune diabetes and B7/CD28 costimulation circumvents that protection  
AUTHOR(S): Balasa, Balaji; Boehm, Bernhard O.; Fortnagel, Anja; Karges, Wolfram; Van Gunst, Kurt; Jung, Nadja; Camacho, Stephanie A.; Webb, Susan R.; Sarvetnick, Nora  
CORPORATE SOURCE: Department of Immunology, The Scripps Research Institute, La Jolla, CA, 92037, USA  
SOURCE: Clinical Immunology (San Diego, CA, United States) (2001), 99(2), 241-252  
CODEN: CLIIYF; ISSN: 1521-6616  
PUBLISHER: Academic Press  
DOCUMENT TYPE: Journal  
LANGUAGE: English

AB The nonobese diabetic (NOD) mouse develops spontaneous T-cell-dependent autoimmune diabetes. The authors tested here whether vaccination of NOD mice with a plasmid DNA encoding glutamic acid decarboxylase (GAD), an initial target islet antigen of autoimmune T cell repertoire, would modulate their diabetes. Our results showed that vaccination of young or old female NOD mice with the GAD-plasmid DNA, but not control-plasmid DNA, effectively prevented their diabetes, demonstrating that GAD-plasmid DNA vaccination is quite effective in abrogating diabetes even after the development of insulitis. The prevention of diabetes did not follow the induction of immunoregulatory Th2 cells but was dependent upon CD28/B7 costimulation. Our results suggest a potential for treating spontaneous autoimmune diabetes via DNA vaccination with plasmids encoding self-Ag.  
(c) 2001 Academic Press.

REFERENCE COUNT: 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 3 OF 6 MEDLINE DUPLICATE 2  
ACCESSION NUMBER: 1999179008 MEDLINE  
DOCUMENT NUMBER: 99179008 PubMed ID: 10077630  
TITLE: Intercellular adhesion molecule-1 inhibits interleukin 4 production by naive T cells.  
AUTHOR: Lukach C R; Wingqvist O; Ozaki M E; Karlsson L;  
Jackson M R; Peterson P A; Webb S  
R  
CORPORATE SOURCE: Department of Immunology, IMM4, The Scripps Research Institute, 10550 North Torrey Pines Road, La Jolla, CA 92037, USA.  
CONTRACT NUMBER: CA25803 (NCI)  
CA41993 (NCI)  
+  
SOURCE: PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA, (1999 Mar 16) 96 (6) 3023-8.  
Journal code: 7505876. ISSN: 0027-8424.  
PUB. COUNTRY: United States  
LANGUAGE: English  
FILE SEGMENT: Priority Journals  
ENTRY MONTH: 199905  
ENTRY DATE: Entered STN: 19990601  
Last Updated on STN: 19990601  
Entered Medline: 19990520

AB The type of cytokines produced during T cell responses determines susceptibility or resistance to many pathogens and influences the development of autoimmunity and allergy. To define the role of individual accessory molecules in cytokine production during primary immune responses, Drosophila cell lines expressing murine major histocompatibility complex class II molecules with defined combinations of accessory molecules were used to present peptide antigen to naive T cell receptor transgenic T cells. Significantly, expression of B7-1 or B7-2 without additional accessory molecules led to very high production of interleukin (IL)-4, which contrasted with minimal IL-4 production elicited by conventional antigen presenting cells (APC). However, coexpression of ICAM-1 and B7 on Drosophila APC induced little IL-4, suggesting an inhibitory role for intercellular adhesion molecule-1 (ICAM-1). In support of this idea, stimulation of T cell receptor transgenic T cells with peptide presented by splenic APC devoid of ICAM-1 (from ICAM-1-deficient mice) led to high IL-4 production. Thus, the level of IL-4 production by naive CD4(+) T cells during typical primary responses appears to be controlled, at least in part, by T-APC interactions involving ICAM-1.

L5 ANSWER 4 OF 6 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.  
 ACCESSION NUMBER: 1999:167516 BIOSIS  
 DOCUMENT NUMBER: PREV199900167516  
 TITLE: The role of accessory molecules in regulating cytokine production.  
 AUTHOR(S): Ozaki, M. E. (1); Luksch, C. R.; Wingqvist, O.;  
 Karlsson, L.; Peterson, P. A.; Webb,  
 S. R.  
 CORPORATE SOURCE: (1) Scripps Res. Inst., La Jolla, CA 92037 USA  
 SOURCE: PASEB Journal, (March 12, 1999) Vol. 13, No. 4 PART 1, pp.  
 A628.  
 Meeting Info.: Annual Meeting of the Professional Research Scientists for Experimental Biology 99 Washington, D.C., USA April 17-21, 1999  
 ISSN: 0892-6638.  
 DOCUMENT TYPE: Conference  
 LANGUAGE: English

L5 ANSWER 5 OF 6 CAPLUS COPYRIGHT 2002 ACS  
 ACCESSION NUMBER: 1998:1388 CAPLUS  
 DOCUMENT NUMBER: 128:60716  
 TITLE: MHC class II antigen presentation systems for CD4+ T-cell activation, differentiation, and adoptive immunotherapy  
 INVENTOR(S): Webb, Susan R.; Wingqvist, Ola;  
 Karlsson, Lars; Jackson, Michael R.;  
 Peterson, Per A.  
 PATENT ASSIGNEE(S): Scripps Research Institute, USA; Webb, Susan R.;  
 Wingqvist, Ola; Karlsson, Lars; Jackson, Michael R.;  
 Peterson, Per A.  
 SOURCE: PCT Int. Appl., 141 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9746256	A1	19971211	WO 1997-US8697	19970522
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9732103	A1	19980105	AU 1997-32103	19970522
AU 723355	B2	20000824		
EP 969865	A1	20000112	EP 1997-927709	19970522
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
JP 2000511898	T2	20000912	JP 1998-500616	19970522
US 6355479	B1	20020312	US 1999-194285	19990412
PRIORITY APPLN. INFO.:			US 1996-18175P	P 19960523
			WO 1997-US8697	W 19970522

AB The authors describe a method based on co-expression of selected MHC class II haplotypes in conjunction with one or more accessory molts. (e.g., B7-1) to activate CD4+ T-cells and effect their differentiation to Th1 or Th2 subsets. Co-expression may be performed on solid supports, liposomes, and derivatized or transgenic cell lines. T-cells so activated cells may be suitable for adoptive immunotherapy.

L5 ANSWER 6 OF 6 MEDLINE DUPLICATE 3  
 ACCESSION NUMBER: 96343863 MEDLINE  
 DOCUMENT NUMBER: 96343863 PubMed ID: 8760806  
 TITLE: Differing roles for B7 and intercellular adhesion molecule-1 in negative selection of thymocytes.  
 COMMENT: Comment in: J Exp Med. 1996 Aug 1;184(2):305-9  
 AUTHOR: Kishimoto H; Cai Z; Brunmark A; Jackson M R;  
 Peterson P A; Sprent J  
 CORPORATE SOURCE: Department of Immunology, Scripps Research Institute, La Jolla, California 92037, USA.  
 CONTRACT NUMBER: AI21487 (NIAID)  
 CA25803 (NCI)  
 CA38355 (NCI)  
 +  
 SOURCE: JOURNAL OF EXPERIMENTAL MEDICINE, (1996 Aug 1) 184 (2)  
 531-7.  
 PUB. COUNTRY: Journal code: 2985109R. ISSN: 0022-1007.  
 United States  
 LANGUAGE: Journal; Article; (JOURNAL ARTICLE)  
 FILE SEGMENT: English  
 ENTRY MONTH: Priority Journals  
 199609  
 ENTRY DATE: Entered STN: 19961008  
 Last Updated on STN: 19961008  
 Entered Medline: 19960923

AB To ensure self tolerance, immature thymocytes with high binding affinity for self peptides linked to major histocompatibility complex (MHC) molecules are eliminated in situ via apoptosis (negative selection). The roles of two costimulatory molecules, B7-1 and intercellular adhesion molecule-1 (ICAM-1), in negative selection was examined by studying apoptosis of T cell receptor transgenic CD4+ thymocytes cultured with specific peptides presented by MHC class I-transfected Drosophila cells. When coexpressed on these cells, B7-1 and ICAM-1 act synergistically and cause strong class I-restricted negative selection of thymocytes. When expressed separately, however, B7-1 and ICAM-1 display opposite functions: negative selection is augmented by B7-1, but is inhibited by ICAM-1. It is notable that B7-1 is expressed selectively in the thymic medulla, whereas ICAM-1 is expressed throughout the thymus. Because of this distribution, the differing functions of B7-1 and ICAM-1 may dictate the sites of positive and negative selection. Thus, in the cortex, the presence of ICAM-1, but not B7-1, on the cortical epithelium may preclude or reduce negative selection and thereby promote positive selection. Conversely, the combined expression of B7-1 and ICAM-1 may define the medulla as the principal site of negative selection.

=> dis his

(FILE 'HOME' ENTERED AT 11:52:47 ON 10 JUL 2002)

FILE 'MEDLINE, CAPLUS, EMBASE, BIOSIS' ENTERED AT 11:53:01 ON 10 JUL 2002

L1 14884 S WEBB S?/AU OR WINGVIST O?/AU OR KARLSSON L?/AU OR JACKSON M?/

L2 198 S L1 AND CD4?

L3 185 S L2 NOT CD40

L4 13 S L3 AND (CD80 OR B7.1)

L5 6 DUP REM L4 (7 DUPLICATES REMOVED)

=> s 15 and (ICAM? OR CD102 OR CD50 OR CD54)

L6 5 L5 AND (ICAM? OR CD102 OR CD50 OR CD54)

=> s MHC or CD4 or CD4+

'CD4+' NOT VALID HERE

'CD4+' NOT VALID HERE

'CD4+' NOT VALID HERE

'CD4+' NOT VALID HERE

=> s MHC or CD4?

L7 326975 MHC OR CD4?

=> s 17 not cd40

L8 310771 L7 NOT CD40

=> s 18 and (CD80 OR B7.1)

L9 3374 L8 AND (CD80 OR B7.1)

=> s 19 and (ICAM? OR CD102 OR CD50 OR CD54)

L10 533 L9 AND (ICAM? OR CD102 OR CD50 OR CD54)

=> s 10 and pd<19960523

'19960523' NOT A VALID FIELD CODE

3 FILES SEARCHED...

L11 2412 L0 AND PD<19960523

=> s 110 and pd<19960523

'19960523' NOT A VALID FIELD CODE

3 FILES SEARCHED...

L12 108 L10 AND PD<19960523

=> dup rem 112

PROCESSING COMPLETED FOR L12

L13 53 DUP REM L12 (55 DUPLICATES REMOVED)

=> s 113 and (HLA (1N) dp)

L14 1 L13 AND (HLA (1N) DP)

=>

=> dis l14 ibib abs kwic

L14 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2002 ACS  
 ACCESSION NUMBER: 1995:871237 CAPLUS  
 DOCUMENT NUMBER: 123:254544  
 TITLE: Regulation and function of adhesion molecule expression by human alveolar epithelial cells  
 AUTHOR(S): Cunningham, A. C.; Kirby, J. A.  
 CORPORATE SOURCE: Dep. Surgery, Univ. Newcastle upon Tyne, UK  
 SOURCE: Immunology (1995), 86(2), 279-86  
 CODEN: IMMUAM; ISSN: 0019-2805  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 AB The role of major histocompatibility complex (MHC) and adhesion mol. expression by alveolar epithelium on the modulation of immune responses in the lung is not understood. We have developed efficient methods to isolate, purify and culture human alveolar epithelial cells (type II pneumocytes) in vitro. The expression of MHC and adhesion mols. by isolated, cultured and cytokine-stimulated alveolar epithelial cells was quantified by flow cytometry, and demonstrated the presence T-cell ligands including class I MHC, HLA-DR and HLA-DP, intracellular adhesion mol.-1 (ICAM-1; CD54) and lymphocyte function-assocd. antigen (LFA-3; CD58), but not vascular cell adhesion mol.-1 (VCAM-1) (CD106) or B7 (CD80). The proinflammatory cytokine interferon-gamma. (IFN-gamma.) caused an up-regulation of class I MHC and ICAM-1. In contrast, tumor necrosis factor-alpha. (TNF-alpha.) and interleukin-1-beta. (IL-1-beta.) had little effect on the expression on these surface antigens by human alveolar epithelial cells. The functional activity of alveolar epithelial adhesion mols. was then studied by detg. their ability to bind allogeneic lymphocytes. An increase in lymphocyte adherence to monolayers of alveolar epithelial cells was obsd. following in vitro activation. However, up-regulation of alveolar epithelial counter receptors with the proinflammatory cytokine .gamma.. IFN did not enhance adhesion. The adhesive interaction between CD18 on lymphocytes and ICAM-1 on alveolar epithelial cells was demonstrated by the use of blocking antibodies specific for both ligands. Blockade of LFA-3 on alveolar monolayers also suppressed lymphocyte adherence. In conclusion, alveolar epithelial cells expressed MHC HLA-A,B,C, HLA-DR and -DP, and functional adhesion mols. including ICAM-1 and LFA-1.

SO Immunology (1995), 86(2), 279-86  
 CODEN: IMMUAM; ISSN: 0019-2805  
 AB The role of major histocompatibility complex (MHC) and adhesion mol. expression by alveolar epithelium on the modulation of immune responses in the lung is not understood. We have developed efficient methods to isolate, purify and culture human alveolar epithelial cells (type II pneumocytes) in vitro. The expression of MHC and adhesion mols. by isolated, cultured and cytokine-stimulated alveolar epithelial cells was quantified by flow cytometry, and demonstrated the presence T-cell ligands including class I MHC, HLA-DR and HLA-DP, intracellular adhesion mol.-1 (ICAM-1; CD54) and lymphocyte function-assocd. antigen (LFA-3; CD58), but not vascular cell adhesion mol.-1 (VCAM-1) (CD106) or B7 (CD80). The proinflammatory cytokine interferon-gamma. (IFN-gamma.) caused an up-regulation of class I MHC and ICAM-1. In contrast, tumor necrosis factor-alpha. (TNF-alpha.) and interleukin-1-beta. (IL-1-beta.) had little effect on the expression on these surface antigens by human alveolar epithelial cells. The functional activity of alveolar epithelial adhesion mols. was then studied by detg. their ability to bind allogeneic lymphocytes. An increase in lymphocyte adherence to monolayers

of alveolar epithelial cells was obsd. following in vitro activation. However, up-regulation of alveolar epithelial counter receptors with the proinflammatory cytokine .gamma.-IFN did not enhance adhesion. The adhesive interaction between CD18 on lymphocytes and ICAM-1 on alveolar epithelial cells was demonstrated by the use of blocking antibodies specific for both ligands. Blockade of LFA-3 on alveolar monolayers also suppressed lymphocyte adherence. In conclusion, alveolar epithelial cells expressed MHC HLA-A,B,C, HLA-DR and -DP, and functional adhesion mols. including ICAM-1 and LFA-3.

- IT Histocompatibility antigens  
RL: MPM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative)  
(HLA-DP, regulation and function of adhesion mol. expression by human alveolar epithelial cells)
- IT Glycoproteins, specific or class  
RL: MPM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative)  
(ICAM-1 (intercellular adhesion mol. 1), regulation and function of adhesion mol. expression by human alveolar epithelial cells)

=> dis his

(FILE 'HOME' ENTERED AT 11:52:47 ON 10 JUL 2002)

FILE 'MEDLINE, CAPLUS, EMBASE, BIOSIS' ENTERED AT 11:53:01 ON 10 JUL 2002  
L1 14884 S WEBB S?/AU OR WINGVIST O?/AU OR KARLSSON L?/AU OR JACKSON M?/  
L2 198 S L1 AND CD4?  
L3 185 S L2 NOT CD40  
L4 13 S L3 AND (CD80 OR B7.1)  
L5 6 DUP REM L4 (7 DUPLICATES REMOVED)  
L6 5 S L5 AND (ICAM? OR CD102 OR CD50 OR CD54)  
L7 326975 S MHC OR CD4?  
L8 310771 S L7 NOT CD40  
L9 3374 S L8 AND (CD80 OR B7.1)  
L10 533 S L9 AND (ICAM? OR CD102 OR CD50 OR CD54)  
L11 2412 S L0 AND PD<19960523  
L12 108 S L10 AND PD>19960523  
L13 53 DUP REM L12 (55 DUPLICATES REMOVED)  
L14 1 S L13 AND (HLA (1N) DP)

=> dis l13 1-53 ibib abs

L13 ANSWER 1 OF 53 CAPLUS COPYRIGHT 2002 ACS  
ACCESSION NUMBER: 1996:357220 CAPLUS  
DOCUMENT NUMBER: 125:31912  
TITLE: Methods for engineering antigen-presenting cells  
INVENTOR(S): Tykocinski, Mark L.  
PATENT ASSIGNEE(S): USA  
SOURCE: PCT Int. Appl., 64 pp.  
CODEN: PIXXD2  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9612009	A2	19960425	WO 1995-US12718	19951011 <-
WO 9612009	A3	19961010		

W: CA, JP  
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE  
PRIORITY APPLN. INFO.: US 1994-324125 19941014  
AB A protein transfer method for producing a cell having a defined MHC: nominal antigen peptide or costimulator on its membrane. The method comprises (1) first contacting the external portion of the cells with an externally applied artificial lipid-modified MHC polypeptide able to bind a nominal antigen peptide, and (2) second contacting the cells with the nominal antigen peptide so that the artificial lipid-modified MHC polypeptide binds the antigen peptide. Demonstrated in examples were prodn. of glycosylphosphatidylinositol-modified human class I MHC, purifn. of HLA-A2.1:GPI/.beta.2m heterodimers, cytolytic T lymphocyte recognition of CLR cells coated with HLA-A2.1:GPI/.beta.2m heterodimer and HLA-A2.1-restricted peptide complexes, prepn. of veto cell by protein transfer of an HLA-A2.1:GPT/.beta.2m peptide complex, treatment of chronic active hepatitis patient with hepatitis B virus-specific T cells amplified using HLA-A2.1:GPI:hepatitis B virus peptide-coated dendritic cells, and a functional artificial GPI-modified costimulator (B7-1 :GPI).

L13 ANSWER 2 OF 53 CAPLUS COPYRIGHT 2002 ACS DUPLICATE 1  
ACCESSION NUMBER: 1996:747032 CAPLUS  
DOCUMENT NUMBER: 126:30062  
TITLE: Transfected Drosophila cells as a probe for defining the minimal requirements for stimulating unprimed CD8+ T cells  
AUTHOR(S): Cai, Zeling; Brunmark, Anders; Jackson, Michael R.;  
Loh, Dennis; Peterson, Per A.; Sprent, Jonathan  
CORPORATE SOURCE: Dep. Immunol., Scripps Res. Inst., La Jolla, CA,  
92037, USA  
SOURCE: Proceedings of the National Academy of Sciences of the United States of America (1996), 93(25), 14736-14741  
CODEN: PNASA6; ISSN: 0027-8424  
DOCUMENT TYPE: National Academy of Sciences  
Journal  
LANGUAGE: English  
AB Stimulation of naive T cells by antigen-presenting cells (APC) is thought to involve two qual. different signals: signal one results from T-cell receptor (TCR) recognition of antigenic peptides bound to major histocompatibility complex (MHC) mols., whereas signal two reflects contact with one or more costimulatory mols. The requirements for stimulating naive T cells were studied with MHC class I-restricted CD8+ T cells from a T-cell receptor transgenic line, with defined peptides as antigen and transfected Drosophila cells as APC. Three main findings are reported. First, stimulation of naive T cells via signal one alone (MHC plus peptide) was essentially nonimmunogenic; thus T cells cultured with peptides presented by MHC class I-transfected Drosophila APC lacking costimulatory mols. showed little or no change in their surface phenotype. Second, cotransfection of two costimulatory mols., B7-1 and

intercellular adhesion mol. 1 (ICAM-1), converted class I+ Drosophila cells to potent APC capable of inducing strong T-proliferative responses and cytokine (interleukin 2) prodn. Third, B7-1 and ICAM-1 acted synergistically, indicating that signal two is complex; synergy between B7-1 and ICAM-1 varied from moderate to extreme and was influenced by both the dose and affinity of the peptide used and the parameter of T-cell activation studied. Transfected Drosophila cells are thus a useful tool for examg. the minimal APC requirements for naive T cells.

L13 ANSWER 3 OF 53 CAPLUS COPYRIGHT 2002 ACS DUPLICATE 2  
ACCESSION NUMBER: 1996:358345 CAPLUS  
DOCUMENT NUMBER: 125:31828  
TITLE: Phenotypic changes in Langerhans' cells after infection with arboviruses: a role in the immune response to epidermally acquired viral infection?  
AUTHOR(S): Johnston, Linda J.; Halliday, Gary M.; King, Nicholas J. C.  
CORPORATE SOURCE: Dep. Pathol. Med., Univ. Sydney, Sydney, 2006, Australia  
SOURCE: J. Virol. (1996), 70(7), 4761-4766  
CODEN: JOVIAM; ISSN: 0022-538X  
DOCUMENT TYPE: Journal  
LANGUAGE: English  
AB The role of Langerhans cells (LC) in the initiation of an immune response to a viral infection remains unclear. In vivo epidermal infection with the arboviruses West Nile virus and Semliki Forest virus significantly increased the expression of major histocompatibility complex class II antigens, CD54, and CD80 on LC. Thus, during an epidermally acquired viral infection, local LC appear to mature to a phenotype approximating that of lymphoid dendritic cells. This change may be important in the activation of naive T cells and the subsequent clearance of viral infection.

L13 ANSWER 4 OF 53 CAPLUS COPYRIGHT 2002 ACS  
ACCESSION NUMBER: 1996:681588 CAPLUS  
DOCUMENT NUMBER: 125:325706  
TITLE: CD80 (B7.1) and CD54 (intracellular adhesion molecule-1) induce target cell susceptibility to promiscuous cytotoxic T cell lysis  
AUTHOR(S): Nishio, Makoto; Spielman, Julie; Lee, Richard K.; Nelson, Debra L.; Podack, Eckhard R.  
CORPORATE SOURCE: Dep. Microbiol. Immunol., Univ. Miami Sch. Med., Miami, FL, 33136, USA  
SOURCE: J. Immunol. (1996), 157(10), 4347-4353  
CODEN: JOIMAJ; ISSN: 0022-1767  
DOCUMENT TYPE: Journal  
LANGUAGE: English  
AB Overexpression of B7 and intracellular adhesion mol.-1 (ICAM-1) on syngeneic cells triggered MHC-unrestricted lysis by MHC-restricted CD8+ CTL without TCR/CD3 engagement. Both CD28/B7 and LFA-1/ICAM-1 interactions were required for MHC-nonrestricted cytotoxicity. Cytotoxicity was measured in 4-h and 16- to 18-h cytotoxicity assays. B7-ICAM-1 overexpression triggered perforin- and Fas ligand-mediated lysis, while TNF-.alpha. was not elicited in MHC-unrestricted cytotoxicity. These results suggest that target cells may elicit MHC-unrestricted lysis from CTL through up-regulation of membrane adherence and costimulatory receptors.

L13 ANSWER 5 OF 53 CAPLUS COPYRIGHT 2002 ACS DUPLICATE 3  
ACCESSION NUMBER: 1996:282494 CAPLUS  
DOCUMENT NUMBER: 124:314846  
TITLE: Intercellular adhesion molecule-1 is necessary but not sufficient to activate CD4+ T cells. Discovery of a novel costimulator on kidney tubule cells  
AUTHOR(S): Hagerty, David T.  
CORPORATE SOURCE: Dep. Med. Pathol., Washington Univ. Sch. Med., St. Louis, MO, 63110, USA  
SOURCE: J. Immunol. (1996), 156(10), 3652-3659  
CODEN: JOIMAJ; ISSN: 0022-1767  
DOCUMENT TYPE: Journal  
LANGUAGE: English  
AB Kidney tubule cells (KTC) are targets of T lymphocyte injury during allograft rejection and interstitial nephritis. KTC process and present self- and foreign Ags for immune recognition by CD4+ T cells in vivo and in vitro. However, it is not known whether KTC can provide the costimulatory signal required to fully activate CD4+ T cells. Using the MRL/MpJ fas-ltbbcrac.lpr.ltbbcrac. model of lupus interstitial nephritis, we found that KTC did not express the costimulators B7-1 or B7-2. Nevertheless, KTC from both normal and systemically infected mice provided non-B7 costimulation to splenic CD4+ T cells. T cell proliferation was blocked by mabs binding intercellular adhesion mol.-1 (ICAM-1) but not by mAb or fusion proteins binding B7-1, B7-2, heat-stable Ag, or vascular cell adhesion mol.-1. Importantly, ICAM-1 expression was necessary but not sufficient to provide costimulation. The transformed KTC line D3.B7- expressed high levels of ICAM-1 but did not provide costimulation. Interestingly, KTC provided costimulation to splenic T cells but not to a Th1 clone. These results show that freshly isolated KTC can provide non-B7 costimulation to splenic T cells via an unidentified costimulator and ICAM-1. Furthermore, these expts. demonstrate the complex nature of T cell activation and show that at least for splenic T cells, three or more signals may be required for full activation on live APC.

L13 ANSWER 6 OF 53 CAPLUS COPYRIGHT 2002 ACS  
ACCESSION NUMBER: 1996:632279 CAPLUS  
DOCUMENT NUMBER: 125:273089  
TITLE: Naive and effector CD4 T cells differ in their requirements for T cell receptor versus costimulatory signals  
AUTHOR(S): Dubey, Caroline; Croft, Michael; Swain, Susan L.  
CORPORATE SOURCE: Hospital Broussais, INSERM Unit 430, Paris, Fr.  
SOURCE: J. Immunol. (1996), 157(8), 3280-3289  
CODEN: JOIMAJ; ISSN: 0022-1767  
DOCUMENT TYPE: Journal  
LANGUAGE: English  
AB The authors used naive CD4 cells and in vitro-derived Th1 and Th2 effectors from TCR transgenic mice to investigate the requirements of the subsets for TCR signaling and interactions with accessory mols.

Peptide antigens (Ag) and immobilized anti-CD3 were used to provide different TCR signals. Anti-CD28 Ab or a panel of class II+ fibroblasts, expressing no accessory mols. or expressing intracellular adhesion mol.-1, B7-1, or both mols., were used as APC or accessory cells (AC). An efficient naive T cell response required a strong TCR signal (high dose anti-CD3 or peptide) and high levels of multiple synergizing costimulatory signals, while effector cells responded efficiently to anti-CD3 alone. Addn. of AC only slightly augmented the effector responses. Effectors responded to lower doses of peptide than naive cells. However, when peptide-pulsed APC were used to stimulate effectors, requirements varied with the cytokine measured. The prodn. of IL-4 did not require accessory mols. on APC. IL-2 prodn. required interacting APC to express accessory mols., but was little augmented by AC not presenting Ag, suggesting a requirement for noncostimulatory interactions. Proliferation of effectors closely paralleled IL-2 prodn. Prodns. of IFN- $\gamma$ , was intermediate in dependence on accessory mols., and prodn. of IL-5 was nearly as dependent as IL-2. These results establish major differences between the induction of naive and effector responses and document differential requirements for the induction of distinct cytokines, indicating that different cytokines may be produced depending on the context of effector restimulation.

L13 ANSWER 7 OF 53 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1996:565015 CAPLUS

DOCUMENT NUMBER: 125:219233

TITLE:

Rapid induction of tumor necrosis factor cytotoxicity in naive splenic T cells by simultaneous CD80 (B7-1) and CD54 (ICAM-1) co-stimulation

AUTHOR(S): Nishio, Makoto; Podack, Eckhard R.

CORPORATE SOURCE: Dep. Microbiology Immunology, Univ. Miami School Medicine, Miami, FL, USA

SOURCE: Eur. J. Immunol. (1996), 26(9), 2160-2164

DOCUMENT TYPE: CODEN: EJIMAF; ISSN: 0014-2980

JOURNAL: Journal

LANGUAGE: English

AB The co-expression of B7-1 (CD80) and intercellular adhesion mol. (ICAM-1 (CD54) on tumor cells can induce tumor immunity and immunol. memory. We show here that the non-immunogenic tumor lines Lewis lung carcinoma and B16F10 melanoma, co-transfected with B7-1 and ICAM-1, induced cytotoxic levels of membrane tumor necrosis factor (TNF) on naive syngeneic T cells within 24 h. Membrane TNF expression, primarily on CD4 cells, was responsible for tumor cell lysis by naive spleen cells and could be completely abolished by anti-TNF antiserum. It is suggested that the strong induction of TNF cytotoxicity may be important in the establishment of tumor immunity.

L13 ANSWER 8 OF 53 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1996:491349 CAPLUS

DOCUMENT NUMBER: 125:165520

TITLE:

T-T cellular interaction between CD4-CD8-regulatory T cells and T cell clones presenting TCR peptide. Its implications for TCR vaccination against experimental autoimmune encephalomyelitis

AUTHOR(S): Kozovska, Milena F.; Yamamura, Takashi; Tabira, Takeshi

CORPORATE SOURCE: Dep. Demyelinating Dis. Aging, Natl. Cent. Neurol. Psychiatry, Kodaira, Japan

SOURCE: J. Immunol. (1996), 157(4), 1781-1790

DOCUMENT TYPE: CODEN: JOIMA3; ISSN: 0022-1767

JOURNAL: Journal

LANGUAGE: English

AB Regulatory T cells recognizing TCR determinants presumably play a crit. role in the control of exptl. autoimmune encephalomyelitis, a prototype tissue-specific autoimmune disease. This study was initiated to det. whether regulatory T cells can be induced against a V.beta.17a CDR2 peptide (residues 50-68) in SJL/J mice. Although the TCR peptide showed regulatory effects in vivo, the presence of T cells specific for the peptide could not be proven with conventional proliferation assays. Unexpectedly, in the presence of myelin basic protein-specific T clone cells (Tcc), the sensitized spleen cells vigorously proliferated in response to the TCR peptide. The subsequent expt. showed that this was due to the outstanding capability of the Tcc as APC for the exogenous TCR peptide. Using the Tcc as APC, the authors were able to establish V.beta.17a50-68-specific T cell lines from in vivo primed spleen cells. The line cells were MHC class I restricted and dominated by T cells with a distinct surface phenotype (CD4-CD8-V.beta.17a+). Presentation of the peptide by the Tcc was inhibited by treatment with gelonin that could block a MHC class I presentation pathway. The ability of T cells to present the TCR peptide was not related to their Ag specificity, but correlated with the expression levels of MHC class I mols. and adhesion mols. such as intercellular adhesion mol.-1 and B7-1 on their surface. The TCR peptide-specific T cells produced a sol. mediator(s) that is inhibitory for T cell activation and were protective against actively induced exptl. autoimmune encephalomyelitis. These results show that V.beta.17a50-68 vaccination induces regulatory CD4-CD8- T cells that could interact with T cells presenting relevant TCR fragments.

L13 ANSWER 9 OF 53 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1996:982005 CAPLUS

DOCUMENT NUMBER: 124:143273

TITLE:

In vivo blockade of TNF-.alpha. by intravenous infusion of a chimeric monoclonal TNF-.alpha. antibody in patients with rheumatoid arthritis. Short term cellular and molecular effects

AUTHOR(S): Lorenz, Hanns-Martin; Antoni, Christian; Valerius, Thomas; Repp, Roland; Gruenke, Mathias; Schwerdtner, Nives; Nuesslein, Hubert; Woody, Jim; Kalden, Joachim R.; et al.

CORPORATE SOURCE: Dep. Internal Medicine, Univ. Erlangen-Nuremberg, Erlangen, Germany

SOURCE: J. Immunol. (1996), 156(4), 1646-53

DOCUMENT TYPE: CODEN: JOIMA3; ISSN: 0022-1767

JOURNAL: Journal

LANGUAGE: English

AB Due to the unknown etiol. of RA, specific treatment is not available. Recently, in a double-blinded, placebo-controlled clin. trial, in vivo blockade of TNF-.alpha. by a single infusion of a chimeric TNF-.alpha.-blocking mAb, cA2, has proven to be highly effective in the treatment of RA. In parallel to this trial, the authors tested the consequences of cA2 infusion in ex vivo and in vitro expts. In this

paper, the authors describe an increase in CD4+ and CD8+ T lymphocyte counts on day 1 and a marked decrease in monocyte counts preferentially on day 7 after cA2 treatment, without major changes in B lymphocyte or NK cell counts. In addn., the authors found an increased responsiveness of PBMC to CD28 mAb/PMA, but not to CD3 mAb, superantigen staphylococcus enterotoxin B, or PHA on day 1 after infusion. The increase in DNA synthesis of PBMC was paralleled by increased IL-2 mRNA and IL-4 mRNA expression and IL-2 protein secretion in culture supernatants after in vitro stimulation of PBMC with CD28 mAb/PMA. In PBMC, the authors did not find any significant changes in mRNA or protein expression of CD28 Ag or CD28 ligands, B7-1 and B7-2. Serum concns. of IL-1-beta., IL-6, and sol. CD14 were significantly diminished after in vivo TNF-.alpha. blockade. The authors did not see relevant changes in granulocyte function in vitro after cA2 infusion. Finally, the authors obsd. a statistically significant decrease in sICAM-1 mols. in the serum of patients treated with serum compared with that in the serum of subjects given placebo. This change in sICAM-1 concn. was evident on days 1 and 7 after the infusion of 10 mg/kg cA2, whereas it occurred only on day 7 in the serum of patients treated with the low dose (1 mg/kg) of cA2.

L13 ANSWER 10 OF 53 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.

ACCESSION NUMBER: 1996:424502 BIOSIS

DOCUMENT NUMBER: PREV1969915558

TITLE: Expression of costimulatory molecules in human leukemias.  
AUTHOR(S): Hirano, N.; Takahashi, T.; Takahashi, T.; Otake, S.;

Hirashima, K.; Emi, N.; Saito, K.; Hirano, M.; Shinohara, K.; Takeuchi, M.; Taketazu, F.; Tsunoda, S.; Ogura, M.;

Omine, M.; Saito, T.; Yazaki, Y.; Ueda, R.; Hirai, H. (1)

CORPORATE SOURCE: (1) Third Dep. Intern. Med., Fac. Med., Univ. Tokyo, Hongo 7-3-1, Bunkyo-ku, Tokyo Japan

SOURCE: Leukemia (Basingstoke), (1996) Vol. 10, No. 7, pp. 1168-1176.

ISSN: 0887-6924.

DOCUMENT TYPE: Article

LANGUAGE: English

AB In order to determine the indication of B7 (B7-1 and B7-2) molecules-mediated immuno-gene therapy for human leukemias, we investigated 94 human leukemic samples for the expression of MHC molecules required for tumor antigen-specific signals and of B7-1, B7-2, and ICAM-1 molecules required for non-specific costimulatory signals. All samples were strongly positive for MHC class I and B4t for class II antigen. B7-1, B7-2 and ICAM-1 were expressed in 5%, 22% and 16% of the total cases, respectively. Especially in 54 AML samples, B7-1 was only expressed in one case, while B7-2 was detected in as many as 15 cases (28%). We have also examined 13 human myelo/monocytic cell lines for the expression of class II and costimulatory molecules and found that significant expression of costimulatory molecules was induced in human leukemic cells by some suitable drugs, among which interferon-gamma (IFN-gamma) was the most potent inducer. Our results indicate that when the B7-mediated immuno-gene therapy was applied to human leukemias, especially to AML, B7-1 was rather preferable to B7-2 in that the latter was more widely expressed on human leukemic cells. Furthermore, since gene-transfer systems occasionally accompany serious problems, it should be taken into account that costimulatory molecules on human myelo/monocytic leukemic cells could be induced ex vivo without the introduction of exogenous genes.

L13 ANSWER 11 OF 53 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1996:305664 CAPLUS

DOCUMENT NUMBER: 125:7787

TITLE: Specific acceptance of cardiac allografts after treatment with antibodies to CD80 and CD86 in mice

AUTHOR(S): Bashuda, H.; Seino, K.; Kano, M.; Sato, K.; Azuma, M.; Yagita, H.; Okumura, K.

CORPORATE SOURCE: School Medicine, Juntendo University, Tokyo, 113, Japan

SOURCE: Transplant. Proc. (1996), 28(2), 1039-1041

CODEN: TRPPA8; ISSN: 0041-1345

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Recent studies have demonstrated that administration of monoclonal antibodies to some intercellular adhesion molts., such as LFA-1/ICAM-1, CD2/CD48, or VLA-4/VCAM-1, led to an indefinite allograft survival. In this study, the authors show that treatment with anti-CD80/CD86 Mabs could induce allospecific tolerance in a murine cardiac transplantation model.

L13 ANSWER 12 OF 53 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.

ACCESSION NUMBER: 96189746 EMBASE

DOCUMENT NUMBER: 1996189746

TITLE: Availability of autologous antigen presenting cells for peptide vaccine therapy.

AUTHOR: Yamasaki S.

CORPORATE SOURCE: First Department of Surgery, Kyoto University, 54 Kawara-cho, Sakyō-ku, Kyoto 606, Japan

SOURCE: Biotherapy, (1996) 10/5 (765-767).

COUNTRY: Japan

DOCUMENT TYPE: Journal; Conference Article

FILE SEGMENT: 016 Cancer

026 Immunology, Serology and Transplantation

LANGUAGE: Japanese

SUMMARY LANGUAGE: English; Japanese

AB We show that a population of cells, derived from the monocyte/macrophage lineage from peripheral blood and grown in granulocyte/macrophage-colony-stimulating factor, exhibits many essential characteristics of professional APC (dendritic type morphology with high levels of MHC class I and II molecules, C D1b, CD54 and CD80 molecules). These cells have a strong co stimulatory function with TCR-stimulated T lymphocytes and are capable of efficiently presenting the nonapeptide (RADPGH-SY), encoded by the melanoma antigen MAGE-1 gene, to the MAGE-1-specific CTL clone 82/30. These results suggest that this type of autologous ex vivo cultured APC, when pulsed with the relevant CTL-determined peptide, can serve as a novel type of candidate vaccine for active specific immunization.

L13 ANSWER 13 OF 53 CAPLUS COPYRIGHT 2002 ACS DUPLICATE 5

ACCESSION NUMBER: 1996:340157 CAPLUS

DOCUMENT NUMBER: 125:31679

TITLE: Development and characterization of a novel monoclonal

antibody (mNI-11) that induces cell adhesion of the LPS-stimulated human monocyte-like cell line U937  
AUTHOR(S): Ikewaki, Nobunao; Inoko, Hidetoshi  
CORPORATE SOURCE: Dep. of Microbiology, Tokai University School of Medicine, Isehara, Japan  
SOURCE: J. Leukocyte Biol. (1996), 59(5), 697-708  
DOCUMENT TYPE: CODEN: JLBIET; ISSN: 0741-5400  
LANGUAGE: Journal English  
AB A monoclonal IgG1 antibody (mAb), designated mNI-11, was produced by immunizing mice with the lipopolysaccharide (LPS)-stimulated monocyte-like cell line U937. The reactivity of mNI-11 was tested by the indirect immunofluorescence method. The antigen defined by mNI-11 was expressed on U937 cells, LPS-stimulated U937 cells, normal CD14+ cells (monocytes/macrophages), and human umbilical vein endothelial cells (HUVECs). Expression of the antigen defined by mNI-11 on HUVECs slightly increased in response to exposure to tumor necrosis factor-.alpha. (TNF-.alpha.) and phorbol myristate acetate (PMA). When the reactivity of mNI-11 and mAbs binding human differentiation antigens such as CD1a, CD11b, CD11c, CD14, CD16, CD18, CD23, CD28, CD29, CD31, CD43, CD44, CD45RA, CD49d, CD50, CD54, CD58, CD80, CD102, CD106, HLA-class I, or HLA-class II antigen was compared, no mNI-11 reactivity resembling that of these mAbs was found. mNI-11 markedly induced homotypic cell aggregation of U937 cells when they were stimulated with LPS. The mNI-11-induced aggregation of LPS-stimulated U937 cells, referred to as LPS-U937 cells, required neither Fc receptor engagement nor crosslinking of the antigen defined by mNI-11 because aggregation was induced by both F(ab')2 fragments and monovalent F(ab') fragments of mNI-11. The mNI-11-induced aggregation was blocked by the addn. of EDTA, and also when incubated at 4 degree.. Mabs to CD11a/CD18 (lymphocyte-function assocd. antigen-1; LFA-1) and CD54 (intercellular adhesion mol.-1; ICAM-1) completely blocked the LPS-U937 cell aggregation induced by mNI-11. The LPS-U937 cell aggregation induced by mNI-11 was partially but not completely blocked by the protein kinase C inhibitor sphingosine and H-7, and was completely blocked by the protein-tyrosine kinase inhibitor genistein. Interestingly, mNI-11 markedly promoted LPS-U937 cell adhesion to HUVECs. The mNI-11 induced LPS-U937 cell adhesion to HUVECs was not reduced in the presence of LFA-1 (CD11a/CD18) or ICAM-1 (CD54) mAbs. LPS-U937 cells, whether treated with mNI-11 or not, sufficiently adhered to the extracellular matrix protein fibronectin, but not to laminin or collagen type I. However, mNI-11 did not markedly promote LPS-U937 cell adhesion to fibronectin. Adhesion of LPS-U937 cells treated with mNI-11 to fibronectin was completely blocked by CD29 (.beta. chain of very late antigens) mAb. The surface antigen recognized by mNI-11 had a mol. size of .apprx.97 kDa under non-reducing conditions and .apprx.117 kDa under reducing conditions, as detd. by immunoblotting anal. The authors found that mNI-11 recognizes an adhesion-assocd. mol. distinct from any previously reported in terms of its pattern of cellular distribution and mol. wt., and also found that mNI-11 has activity which induces cell adhesion/aggregation of U937 cells when stimulated with LPS.

L13 ANSWER 14 OF 53 CAPLUS COPYRIGHT 2002 ACS DUPLICATE 6  
ACCESSION NUMBER: 1996:584820 CAPLUS  
DOCUMENT NUMBER: 125:245461  
TITLE: Immunogenicity of biliary epithelium: Investigation of antigen presentation to CD4+T cells  
AUTHOR(S): Leon, Maria P.; Bassendine, Margaret F.; Wilson, Julia L.; Ali, Simi; Thick, Michael; Kirby, John A.  
CORPORATE SOURCE: Medical School, University Newcastle upon Tyne, Newcastle upon Tyne, NE2 4HH, UK  
SOURCE: Hepatology (Philadelphia) (1996), 24(3), 561-567  
DOCUMENT TYPE: CODEN: HPTLD9; ISSN: 0270-9139  
LANGUAGE: Journal English  
AB The intrahepatic biliary epithelium is susceptible to extensive T-cell-mediated damage during primary biliary cirrhosis, primary sclerosing cholangitis, and hepatic allograft rejection. During these processes, human intrahepatic biliary epithelial cells (HIBEC) become activated and express high levels of the lymphocyte adhesion mol., intercellular adhesion mol.-1 (ICAM-1) and lymphocyte-assocd. antigen (LFA)-3, and of class II MHC antigens. It follows that activated HIBEC may also play a direct role in the activation of antigen-specific CD4+ T lymphocytes. The capacity of class II MHC antigen-expressing HIBEC to present antigen and induce specific proliferation of CD4+ T cells was exmd. in this study. Lines of purified HIBEC were activated by culture with the proinflammatory cytokines interferon gamma (IFN-.gamma.) and tumor necrosis factor .alpha. and were mixed in coculture with allogeneic CD4+ T cells. The result of interaction between these cells was assessed by measurement of lymphoproliferation and IL-2 prodn. Class II MHC antigen-expressing HIBEC failed to induce either lymphoproliferation or IL-2 prodn. However, both of these parameters of T-cell activation were pos. in cocultures when a costimulation signal was delivered to T cells by adding bivalent anti-CD28 antibodies. The antigen-specific activation of these T cells was further enhanced by the addn. of a crosslinking secondary antibody that caused CD28 receptor aggregation. The failure of cytokine-stimulated HIBEC to induce T-cell activation is consistent with the observation that HIBEC do not express the costimulatory CD28 ligands B7-1 or B7-2 at either mRNA or protein levels. It may be concluded that HIBEC are unlikely to play a direct role in activation of antigen-specific CD4+ T lymphocytes within the inflamed liver.

L13 ANSWER 15 OF 53 CAPLUS COPYRIGHT 2002 ACS DUPLICATE 7  
ACCESSION NUMBER: 1996:504816 CAPLUS  
DOCUMENT NUMBER: 125:165648  
TITLE: Differing roles for B7 and intercellular adhesion molecule-1 in negative selection of thymocytes  
AUTHOR(S): Kishimoto, Hidehiro; Cai, Zeling; Brunmark, Anders; Jackson, Michael R.; Peterson, Per A.; Sprent, Jonathan  
CORPORATE SOURCE: Dep. Immunol., Scripps Res. Inst., La Jolla, CA, 92037, USA  
SOURCE: J. Exp. Med. (1996), 184(2), 531-537  
DOCUMENT TYPE: CODEN: JEMEAV; ISSN: 0022-1007  
LANGUAGE: Journal English  
AB To ensure self tolerance, immature thymocytes with high binding affinity for self peptides linked to major histocompatibility complex (MHC) mols. are eliminated in situ via apoptosis (neg. selection). The roles

of two costimulatory mol., B7-1 and intercellular adhesion mol.-1 (ICAM-1), in neg. selection was exmd. by studying apoptosis of T cell receptor transgenic CD4+8+ thymocytes cultured with specific peptides presented by MHC class I-transfected Drosophila cells. When coexpressed on these cells, B7-1 and ICAM-1 act synergistically and cause strong class I-restricted neg. selection of thymocytes. When expressed sep., however, B7-1 and ICAM-1 display opposite functions: neg. selection is augmented by B7-1, but is inhibited by ICAM-1. It is notable that B7-1 is expressed selectively in the thymic medulla, whereas ICAM-1 is expressed throughout the thymus. Because of this distribution, the differing functions of B7-1 and ICAM-1 may dictate the sites of pos. and neg. selection. Thus, in the cortex, the presence of ICAM-1, but not B7-1, on the cortical epithelium may preclude or reduce neg. selection and thereby promote pos. selection. Conversely, the combined expression of B7-1 and ICAM-1 may define the medulla as the principal site of neg. selection.

L13 ANSWER 16 OF 53 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.  
ACCESSION NUMBER: 1997:159793 BIOSIS  
DOCUMENT NUMBER: PREV199799458996  
TITLE: MHC class II-mediated antigen presentation by melanoma cells.  
AUTHOR(S): Brady, Mary S. (1); Eckels, David D.; Ree, Sophia Y.; Schultheiss, Kim E.; Lee, Janet S.  
CORPORATE SOURCE: (1) Memorial Sloan-Kettering Cancer Cent., 1275 York Avenue, New York, NY 10021 USA  
SOURCE: Journal of Immunotherapy with Emphasis on Tumor Immunology, (1996) Vol. 19, No. 6, pp. 387-397.  
ISSN: 1067-5582.

DOCUMENT TYPE: Article  
LANGUAGE: English  
AB Constitutive expression of major histocompatibility complex (MHC) class II molecules is normally restricted to professional antigen-presenting cells (APCs) of the immune system, although it also occurs frequently in melanoma. Clinical evidence suggesting that MHC class II expression by melanoma is associated with tumor progression led us to postulate a role for MHC class II-mediated antigen presentation in this disease. First, we investigated whether melanoma cells derived from metastases can process antigen and/or present peptide via MHC class II molecules to a peptide-specific CD4+ T-cell clone. In all cell lines tested, melanoma cells were able to process antigen and present peptide efficiently to CD4+ T cells, resulting in T-cell proliferation increased 5-26-fold over controls. Next, we found that CD28-mediated costimulation was not required, because blocking with CTLA4Ig had no effect on the T-cell response to either melanoma or B cells as APCs. In contrast, blocking CD54 (ICAM-1) resulted in a decrease in proliferation in response to peptide presentation by melanoma but not B cells. These data demonstrate that MHC class II molecules on melanoma cells are functional and that antigen-processing pathways are intact. In addition, CD54 seems to play a significant role in peptide presentation by melanoma.

L13 ANSWER 17 OF 53 CAPLUS COPYRIGHT 2002 ACS DUPLICATE 8  
ACCESSION NUMBER: 1996:501042 CAPLUS  
DOCUMENT NUMBER: 125:192838  
TITLE: New insights into tumor-host interactions in lymphoma metastasis  
AUTHOR(S): Umansky, V.; Schirrmacher, V.; Rocha, M.  
CORPORATE SOURCE: Div. Cellular Immunology, German Cancer Research Center, Heidelberg, D-69120, Germany  
SOURCE: J. Mol. Med. (Berlin) (1996), 74(7), 353-363  
CODEN: JMLMB8; ISSN: 0946-2716  
DOCUMENT TYPE: Journal; General Review  
LANGUAGE: English  
AB A review with 122 refs. on the interactions of metastasized tumor cells with their microenvironment in target organs. The recent literature and own data about the expression of costimulatory (MHC class II, CD80, sialoadhesin) and adhesion (LFA-1, ICAM-1, VLA-4) mol. on both metastasized tumor cells and host cells and about the prodn. of nitric oxide by in situ activated Kupffer and endothelial cells in the process of liver metastasis are reviewed and discussed.

L13 ANSWER 18 OF 53 CAPLUS COPYRIGHT 2002 ACS DUPLICATE 9  
ACCESSION NUMBER: 1996:125795 CAPLUS  
DOCUMENT NUMBER: 124:173266  
TITLE: Cultured human Langerhans' cells are superior to fresh cells at presenting native HIV-1 protein antigens to specific CD4+ T-cell lines  
AUTHOR(S): Girolomoni, G.; Valle, M. T.; Zacchi, V.; Costa, M. G.; Giannetti, A.; Manca, F.  
CORPORATE SOURCE: Istituto Dermopatico dell'Immunocologata, IRCCS, Rome, Italy  
SOURCE: Immunology (1996), 87(2), 310-16  
CODEN: IMMUAM; ISSN: 0019-2805  
DOCUMENT TYPE: Journal  
LANGUAGE: English  
AB Cultured Langerhans' cells (CLC) exhibit enhanced antigen-presenting function compared to freshly isolated LC (FLC), but they are commonly believed to be inefficient at processing intact proteins. In this study, FLC and CLC from normal, human immunodeficiency virus (HIV) seroneg. volunteers were compared for their ability to present the HIV-1 envelope glycoprotein gp120 or reverse transcriptase (p66) antigens to autologous, specific CD4+ T cell lines. Epidermal cell suspensions enriched for LC were prep'd. from suction blister roofs. FLC stimulated T cells at lower antigen concns. compared to unfractionated peripheral blood mononuclear cells (PBMC). CLC were more potent on a per cell basis than FLC, PBMC or adherent monocytes at presenting native gp120, native p66 or immunogenic peptides. CLC were also more efficient than FLC or PBMC in terms of the amt. of antigen required for T-cell activation. Chloroquine and leupeptin inhibited presentation of intact p66, but not of an immunodominant peptide, by FLC or CLC, thus indicating that both cells utilize antigen processing mechanisms that are based on intracellular acidification and protease activity. Incubation of CLC with monoclonal antibodies against HLA-DR, CD11b, CD18, CD50, CD54, CD58 or CD80, but not anti-major histocompatibility complex class I (MHC-I), inhibited antigen-specific T-cell proliferation to varying degrees. We conclude that human CLC retain the ability to process and present protein antigens potently to CD4+ T cells. Thus, CLC have the capacity to participate actively in the generation and

maintenance of T-helper cell immunity to viral antigens during HIV-1 infection.

L13 ANSWER 19 OF 53 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.  
ACCESSION NUMBER: 1996:509588 BIOSIS  
DOCUMENT NUMBER: PRV199699231944  
TITLE: Regulation of Langerhans cell function via blood borne factor(s).  
AUTHOR(S): Xie, Yong; Streilein, J. Wayne (1)  
CORPORATE SOURCE: (1) Dep. Dermatol., Harvard Med. Sch., 20 Staniford St., Boston, MA 02114 USA  
SOURCE: Journal of Dermatological Science, (1996) Vol. 12, No. 3, pp. 263-274.  
ISSN: 0923-1811.  
DOCUMENT TYPE: Article  
LANGUAGE: English

AB Langerhans cells (LC) are epidermal dendritic cells that are functionally labile. Freshly obtained LC (fLC) readily activate allogeneic T cells, but they are incapable of activating autologous T cells; and even when pulsed with antigen, they fail to activate naive, antigen-specific T cells. When fLC are cultured for 2-3 days in the presence of keratinocytes, LC swiftly up-regulate surface expression of class I and II MHC molecules, and express de novo the co-stimulatory molecules B7 and ICAM-1. In addition to displaying enhanced ability to activate allogeneic T cells, cultured LC acquire the novel functional property of activating autologous T cells. It is believed that keratinocyte-derived GM-CSF is the primary driving force responsible for the conversion of fresh to cultured LC in vitro. However, in vivo administration of GM-CSF, either intracutaneously or systemically, fails to induce LC to undergo functional transformation *in situ*. Moreover, despite a high level of GM-CSF in the circulation, fLC from mice bearing GM-CSF-producing tumors display no ability to activate syngeneic T cells. These observations suggest that a homeostatic factor that antagonizes the effect of GM-CSF may be present in vivo. To test this possibility, we have examined the functional properties of LC prepared from mouse skin that had been explanted *in vitro* for 3 days. We found that the functional and phenotypic features of these cells closely resembled those of LC cultured in single cell suspension: the cells strongly expressed B7-1 and B7-2, and displayed enhanced expression of class II MHC molecules; they readily activated naive autologous T cells. Strikingly, when explants or suspensions of fresh epidermal cells were cultured in the presence of 10% mouse serum they failed to acquire syngeneic T cell activating properties; and surface up-regulation of la and de novo expression of B7 was inhibited. However, the cultured cells still expressed surface la and readily activated allogeneic naive T cells. If mouse serum was added only during the last 24 h of culture, the LC displayed full functional transformation. Human, rabbit and bovine serum showed no inhibitory effect on mouse LC. Our data suggest that mouse serum contains a factor (or factors) that inhibits, in a species-specific manner, epidermal LC from undergoing functional transformation *in vitro*, and this factor may maintain epidermal LC in the 'fresh' functional program *in vivo*.

L13 ANSWER 20 OF 53 CAPLUS COPYRIGHT 2002 ACS DUPLICATE 10  
ACCESSION NUMBER: 1996:450503 CAPLUS  
DOCUMENT NUMBER: 125:140301  
TITLE: Antigen-presenting-cell function of interferon .gamma.-treated human gingival fibroblasts  
AUTHOR(S): Shimabukuro, Yoshiro; Murakami, Shinya; Okada, Hiroshi  
CORPORATE SOURCE: Faculty Dentistry, Osaka University, Suita, 565, Japan  
SOURCE: J. Periodontal Res. (1996), 31(3), 217-228  
CODEN: JPDRAY; ISSN: 0022-3484  
DOCUMENT TYPE: Journal  
LANGUAGE: English

AB The present study was carried out to examine the antigen-presenting cell (APC) functions of human gingival fibroblasts (HGF) elicited with IFN-gamma.. Stimulation of HGF with IFN-gamma. clearly induced HLA-DR expression and enhanced expression of intercellular adhesion mol.-1 (ICAM-1) on HGF. Despite the phenotypical resemblance of IFN-gamma.-treated HGF to so-called APC, HLA-DR pos. HGF were unable to induce proliferation of allo-reactive peripheral blood T cells (PBT) isolated from different donors. The failure of IFN-gamma.-treated HGF to stimulate unprimed allo-reactive PBT was not due to the lack of prodn. of IL-1 or the immunosuppressive effect of PGE2 from HGF. The fact that detectable expression of CD80, ligand for CD28, was not found on IFN-gamma.-treated HGF may at least in part explain the ineffective function of HGF as APC. Interestingly, IFN-gamma.-treated HGF induced proliferation of primed allo-reactive CD4+ T cells in a HLA-DR dependent manner, suggesting that IFN-gamma.-treated HGF may have the ability to stimulate pre-activated T cells. We then confirmed that high levels of IFN-gamma. mRNA were detectable in inflamed gingival tissue. Although it cannot be concluded from this study that HGF are incapable of effectively presenting antigenic peptides to autologous T cells bearing appropriate T cell receptors, present results suggest that HGF may be affected by locally-secreted IFN-gamma. and that the IFN-gamma.-stimulated HGF may play a role in regulating immune responsiveness in inflammatory periodontal lesions.

L13 ANSWER 21 OF 53 CAPLUS COPYRIGHT 2002 ACS DUPLICATE 11  
ACCESSION NUMBER: 1996:193521 CAPLUS  
DOCUMENT NUMBER: 124:258280  
TITLE: Interferon-.gamma. and tumor necrosis factor-.alpha. treatment of ex vivo human carcinoma cells potentiates their interaction with allogeneic lymphocytes  
AUTHOR(S): Vankay, Farkas; Hising, Christina; Sjoewall, Kerstin;  
CORPORATE SOURCE: Microbiology and Tumor Biology Center, Karolinska Inst., Stockholm, S-171 77, Swed.  
SOURCE: J. Interferon Cytokine Res. (1996), 16(3), 201-7  
CODEN: JICRPF; ISSN: 1079-9907  
DOCUMENT TYPE: Journal  
LANGUAGE: English

AB Short-term exposure of ex vivo carcinoma and sarcoma cells to IFN-.gamma. and TNF-.alpha. induced or elevated to detectable levels the surface expression of MHC class I, class II, and ICAM-1 (CD54), but only rarely the B7 (CD80) mol. The cytokine-treated tumor cells interacted more efficiently with allogeneic blood lymphocytes collected from healthy donors compared with untreated cells. This was demonstrated by the induction of DNA synthesis and generation of cytotoxic activity in mixed cultures, and by the elevated susceptibility to the cytotoxic effectors. Although the cytokine-induced increase in MHC and ICAM-1 on the low-expresser tumors were probably important to the interaction with lymphocytes, it is likely

(FILE 'HOME' ENTERED AT 11:52:47 ON 10 JUL 2002)

FILE 'MEDLINE, CAPLUS, EMBASE, BIOSIS' ENTERED AT 11:53:01 ON 10 JUL 2002  
L1 144884 S WEBB S?/AU OR WINGVIST O?/AU OR KARLSSON L?/AU OR JACKSON M?/  
L2 198 S L1 AND CD4?  
L3 185 S L2 NOT CD40  
L4 13 S L3 AND (CD80 OR B7.1)  
L5 6 DUP REM L4 (7 DUPLICATES REMOVED)  
L6 5 S L5 AND (ICAM? OR CD102 OR CD50 OR CD54)  
L7 326975 S MHC OR CD4?  
L8 310771 S L7 NOT CD40  
L9 3374 S L8 AND (CD80 OR B7.1)  
L10 533 S L9 AND (ICAM? OR CD102 OR CD50 OR CD54)  
L11 2412 S L0 AND PD<19960523  
L12 108 S L10 AND PD<19960523  
L13 53 DUP REM L12 (55 DUPLICATES REMOVED)  
L14 1 S L13 AND (HLA (1N) DP)

that other properties were also induced that contributed to the phenomenon. This was indicated by the results obtained with several tumors that expressed indigenously high levels of these mols. but reacted with the allogeneic lymphocytes only or more efficiently after treatment with IFN-.gamma. and TNF-.alpha.. In these expts. B7 expression did not influence the efficiency of interactions between lymphocyte and tumor cells. Under the conditions used, the untreated tumor cells that did not activate allogeneic lymphocytes were sensitive to appropriately activated effectors. Thus the afferent and efferent arms of lymphocyte-tumor cell interactions appeared to have different requirements.

L13 ANSWER 22 OF 53 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.

ACCESSION NUMBER: 97133287 EMBASE

DOCUMENT NUMBER: 1997133287

TITLE: Human thymic epithelial cells present superantigens to T-cell lines and thymocytes.

AUTHOR: Jorgensen A.; Nielsen M.; Svejgaard A.; Ledbetter J.A.; Odum N.; Ropke C.

CORPORATE SOURCE: C. Ropke, Institute of Medical Anatomy, University of Copenhagen, The Panum Institute, Blegdamsvej 3, DK-2200 Copenhagen N, Denmark. C.Ropke@mail.ku.dk

SOURCE: Experimental and Clinical Immunogenetics, (1996) 13/3-4 (192-203).

Refs: 40

ISSN: 0254-9670 CODEN: ECIME4

COUNTRY: Switzerland

DOCUMENT TYPE: Journal; Article

FILE SEGMENT: 026 Immunology, Serology and Transplantation

LANGUAGE: English

SUMMARY LANGUAGE: English

AB It is generally accepted that thymic epithelial cells (TEC) act as accessory cells in positive selection of pre-T cells. However, our knowledge of the antigen presentation and accessory cell function of human TEC is limited. Here we present results obtained by the use of serum-free cultured human TEC, showing that IFN-.gamma.-treated TEC are able to support T-cell-mediated responses to the bacterial superantigens (Sag) SEA and SEB, even at very low Sag concentrations. T-cell responses to TEC-presented Sag were dependent on the presence of the adhesion molecules ICAM-1, ICAM-2, LFA-1, and LFA-3, but not on CD4 and CD8 molecules. There is a low but significant expression of B7 molecules on human TEC, and treatment of TEC with anti-B7.1 and anti-B7.2 antibodies before Sag pulsing leads to decreased Sag responses, indicating a significant importance of B7 molecules on TEC. Both CD4+ T-cell lines and CD4+ as well as CD8+ subpopulations of thymocytes showed significant responses, whereas nonseparated thymocytes, CD4+8+, and CD4-CD8-thymocytes did not respond or showed very low responses. In conclusion, the present results demonstrate that cultured human TEC are able to present Sag to thymocytes.

L13 ANSWER 23 OF 53 CAPLUS COPYRIGHT 2002 ACS DUPLICATE 12

ACCESSION NUMBER: 1996:650575 CAPLUS

DOCUMENT NUMBER: 125:325816

TITLE: A novel monoclonal antibody mNI-58A against the .alpha.-chain of leukocyte function-associated antigen-1 (LFA-1) blocks the homotypic cell aggregation and actively regulates morphological changes in the phorbol myristate acetate (PMA)-activated human monocyte-like cell line, U937

AUTHOR(S): Ikewaki, N.; Yamada, A.; Sonoda, A.; Inoko, H. School Nursing, Kitasato University, Kanagawa, Japan

CORPORATE SOURCE: Tissue Antigens (1996), 48(3), 161-173

SOURCE: CODEN: TSANA2; ISSN: 0001-2815

DOCUMENT TYPE: Journal

LANGUAGE: English

AB A monoclonal antibody (mAb), designated mNI-58A, was produced by immunizing mice with the lipopolysaccharide (LPS)-stimulated monocyte-like cell line, U937. The antigen defined by mNI-58A was widely expressed on various lymphoid cells and all cell lines examd. except the erythroid cell line, K562. When the reactive patterns between mNI-58A and the mAbs to various human differentiation antigens (CD11a, CD11b, CD11c, CD14, CD16, CD18, CD23, CD28, CD31, CD43, CD44, CD45RA, CD50, CD54, CD58, CD80, CD102, CD106, HLA-class I and -class II antigen) were compared, that of mNI-58A was similar to those of the leukocyte function-assocd. antigen-1 (LFA-1) mAbs. Using a competitive immunofluorescence binding assay it was found that the preincubation with one of the CD11a mAbs, 2F12 completely blocked the subsequent binding of mNI-58A. mNI-58A prevented the homotypic cell aggregation of the phorbol myristate acetate (PMA)-activated U937 cells (referred to as PMA-U937) and PMA-activated Epstein-Barr virus (EBV)-transformed B cell lines, B-85 and Mann. mNI-58A markedly induced the spread formation of the PMA-U937 cells following this blocking of the homotypic cell aggregation, whereas 2F12 did not under the same condition. The spread formation induced by mNI-58A was completely blocked by cytochalasin B (CyB), cytochalasin D (CyD), cycloheximide (CHX) or protein kinase C inhibitors, sphingosine and H-7. The U937 cells markedly adhered to the tumor necrosis factor-.alpha. (TNF-.alpha.)-stimulated human umbilical vein endothelial cells (HUVECs) and also to the extracellular matrix protein, fibronectin, but mNI-58A did not enhance or block these adhesion processes. mNI-58A pptd. two glycoproteins with mol. wt. 180 kDa and 95 kDa as detd. by SDS-PAGE anal., which were identical to the LFA-.alpha. (CD11a) and .beta. (CD18) chains of leukocyte integrin pptd. by the CD11a mAbs, resp. Sequential immunopppn. studies using the CD11a mAb (2F12) also indicate that mNI-58A recognizes an epitope on the .alpha.-chain of the LFA-1 mol. The ability of mNI-58A to block the PMA-U937 cells and to induce the spread formation of these cells suggests that mNI-58A is a novel mAb reacting with an epitope on the .alpha.-chain of LFA-1 different from those recognized with the existing CD11a mAbs.

L13 ANSWER 24 OF 53 CAPLUS COPYRIGHT 2002 ACS DUPLICATE 13

ACCESSION NUMBER: 1996:305803 CAPLUS

DOCUMENT NUMBER: 125:7789

TITLE: Induction of autologous tumor-specific cytotoxic T-lymphocyte activity against a human renal carcinoma cell line by B7-1 (CD80) costimulation

AUTHOR(S): Wang, Yi-Chong; Zhu, Lihua; McHugh, Rebecca; Graham, Sam D. Jr.; Hillyer, Christopher D.; Dillehay, Dirk; Sell, Kenneth W.; Selvaraj, Periasamy School Medicine, Emory University, Atlanta, GA, USA

CORPORATE SOURCE: J. Immunother. Emphasis Tumor Immunol. (1996) 19(1), 1-8

SOURCE: CODEN: JIBIEZ; ISSN: 1067-5582

DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 AB Recently mouse models have shown that expression of costimulatory mol. such as B7-1 on tumor cells can induce tumor-specific immunity, suggesting that tumor cells modified to express costimulatory mol. can be a potential tumor vaccine. To investigate the importance of B7-1 costimulation in induction of autologous tumor immunity in humans, we established a renal carcinoma cell line, RCC-1, from a tumor resection and studied the patient's antitumor immune responses in vitro. The RCC-1 cell line constitutively expressed major histocompatibility complex (MHC) class I, intercellular adhesion mol. (ICAM)-1, and leukocyte function-assoc. antigen (LFA)-3 mol., and MHC class II mol. were induced by interferon-gamma. (IFN-gamma.) treatment in vitro. However, neither RCC-1 nor IFN-gamma.-treated RCC-1 cells expressed B7-1, and both failed to induce T-cell proliferative responses in mixed lymphocyte and tumor cell reaction (MLTR) assays, suggesting that the costimulatory signals provided by cell adhesion mol. such as ICAM-1 and LFA-3 were not sufficient to elicit an antitumor immune response. However, on transfection of the human B7-1 into RCC-1, these cells were able to induce a significant T-cell proliferation in MLTR assays. This T-cell response could be blocked by anti-B7 mAb treatment of the tumor cells. RCC-1B7 cells also induced the generation of tumor-specific cytolytic T lymphocytes to the parent RCC-1 cells in vitro, with little nonspecific cytolysis of an unrelated RCC line, A498, or autologous phytohemagglutinin (PHA) blasts. This specific cytotoxicity could be abrogated by anti-CD28 mAb and complement treatment. In summary, our study indicates that B7-1-CD28 interaction plays a crit. role in induction of autologous tumor-specific cytotoxic T lymphocytes (CTLs) in humans, suggesting that the costimulatory mol. transfected tumor cells could be useful in expanding tumor-specific autologous CTL in vitro for adoptive tumor immunotherapy.

L13 ANSWER 25 OF 53 CAPLUS COPYRIGHT 2002 ACS  
 ACCESSION NUMBER: 1996:142192 CAPLUS

DOCUMENT NUMBER: 124:173443

TITLE: Methods for inhibiting antigen specific T cell responses

INVENTOR(S): Blazar, Bruce R.; Vallera, Daniel A.

PATENT ASSIGNEE(S): Regents of the University of Minnesota, USA

SOURCE: PCT Int. Appl., 61 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9534320	A2	19951221	WO 1995-US7351	19950607 <--
WO 9534320	A3	19960118		
W: AU, CA, JP				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
CA 2191733	AA	19951221	CA 1995-2191733	19950607 <--
AU 9527018	A1	19960105	AU 1995-27018	19950607 <--
EP 784482	A2	19970723	EP 1995-922279	19950607
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
JP 10501815	T2	19980217	JP 1995-502351	19950607
AU 9947458	A1	19991028	AU 1999-47458	19990908
PRIORITY APPLN. INFO.:				
	US 1994-255267		19940607	
	US 1995-472697		19950606	
	AU 1995-27018		19950607	
	WO 1995-US7351		19950607	

AB Methods for inhibiting antigen-specific T cell responses by use of an agent which inhibits a costimulatory signal in T cells are disclosed. Preferably, both a first agent which inhibits a costimulatory signal in the T cell and a second agent which inhibits adhesion of the T cell to a cell presenting antigen to the T cell, are used to inhibit antigen-specific T cell responses. For example, anti-LFA-1 antibody, that inhibits adhesion of a T cell to a cell presenting antigen, can be used in conjunction with a CTLA4-Ig fusion protein which inhibits a costimulatory signal in the T cell. Alternatively, another agent which inhibits a costimulatory signal in T cells, such as an anti-B7-1 antibody or an anti-B7-2 antibody can be used with a second agent which inhibits a proliferative signal in the T cell e.g., an anti-IL-2 receptor antibody. The methods of the invention are particularly useful for inhibiting graft vs. host disease and for inhibiting rejection of a transplanted tissue or organ.

L13 ANSWER 26 OF 53 CAPLUS COPYRIGHT 2002 ACS  
 ACCESSION NUMBER: 1996:113374 CAPLUS

DOCUMENT NUMBER: 124:143577

TITLE: Methods using PCR bridging compounds for the selective modulation of antigen-specific T-cell responsiveness

INVENTOR(S): De Boer, Mark; Barcy, Serge

PATENT ASSIGNEE(S): Innogenetics N.V., Belg.

SOURCE: PCT Int. Appl., 62 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9532734	A1	19951207	WO 1995-EP2012	19950526 <--
W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SI, SK, TJ, TT, UA, US, UZ				
RW: KE, MW, SD, SZ, UG, AT, BE, CH, DB, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
CA 2188812	AA	19951207	CA 1995-2188812	19950526 <--
AU 9526709	A1	19951221	AU 1995-26709	19950526 <--
EP 759782	A1	19970305	EP 1995-921760	19950526
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
PRIORITY APPLN. INFO.:			EP 1994-870088	19940526
			WO 1995-EP2012	19950526

AB The present invention relates to new Fc gamma.RII bridging compns. for impairing the capacity of antigen presenting cells (APCs) to stimulate the activation of antigen-specific T-cells, resulting in modulation of antigen-specific T-cell responsiveness. More particularly, said

Fc.gamma.RII bridging agents are chosen from the group consisting of: aggregated human IgG mols.; aggregated Fc fragments of human IgG mols.; a bivalent monoclonal antibody to the Fc.gamma.RII; a multivalent monoclonal antibody to the Fc gamma.RII; a functionally active fragment of said bivalent or multivalent monoclonal antibody; a recombinant fusion protein of 2 or more human IgG Fc parts; liposome vesicles comprising any of the foregoing, provided that said Fc.gamma.RII compn. prevents the expression of the co-stimulatory mols. B7-1/2 and/or down-modulates the ICAM-3 mol. expression by these professional APCs. The present invention also relates to prophylactic and therapeutic methods and compns. to prevent or treat the rejection of solid organs, tissues and cells after transplantation; for inducing T-cell anergy or T-cell tolerance; for treating allergic diseases; or for the treatment of autoimmune diseases. The present invention also relates to Fc.gamma.RII bridging professional APCs prep'd. by bridging APCs with an Fc.gamma.RII bridging agent according to the present invention. In example, FcR bridging strongly down-modulated expression of B7-1, B7-2, CD14, ICAM-3 and strongly up-regulated expression of CD44. FcR bridging greatly inhibited secretion of interleukin 2, stimulation of resting T cells by monocytes, interaction of B7-1/CD28, proliferation of antigen-specific T cells, etc.

L13 ANSWER 27 OF 53 CAPLUS COPYRIGHT 2002 ACS DUPLICATE 14  
ACCESSION NUMBER: 1995:957728 CAPLUS  
DOCUMENT NUMBER: 124:6596  
TITLE: Dendritic cells generated from peripheral blood transfected with human tyrosinase induce specific T cell activation  
AUTHOR(S): Alijagic, Selma; Moeller, Peter; Artuc, Metin; Jurgovsky, Klaus; Czarnetzki, Beate M.; Schadendorf, Dirk  
CORPORATE SOURCE: Dep. Dermatol., Humboldt Univ. Berlin, Berlin, Germany  
SOURCE: Eur. J. Immunol. (1995), 25(11), 3100-7  
CODEN: EJIMAF; ISSN: 0014-2980  
DOCUMENT TYPE: Journal  
LANGUAGE: English

AB Peptides of melanosomal proteins have recently been shown to be recognized in an HLA-restricted mode by specific cytolytic T lymphocytes in melanoma patients. Dendritic antigen-presenting cells (DC) are considered to be the most effective stimulators of T cell responses, and the use of these cells has therefore been proposed to generate therapeutic responses to tumor antigens in cancer patients. The authors, therefore, generated DC from peripheral blood of normal donors in the presence of granulocyte/macrophage colony-stimulating factor and interleukin-4. Flow cytometric anal. of the cells during a 2-wk culture revealed a loss of CD14 and CD34 expression, a concomitant increase of CD1a, CD11a, b, and c, CD44, CD45, CD54, HLA-class I and II, and intermediate levels of CD26, CD80, and CD86. Cultured DC stimulated proliferation of allogeneic T cells and induced a marked, up to 20-fold, stimulation of T cell proliferation after pulsing with tetanus toxoid. To achieve independence of already-identified antigenic peptides presented in HLA class I-restricted fashion, which limits the general applicability of such peptides for vaccination of melanoma patients, the authors tested whether DC are transfectable with eukaryotic expression plasmids. DC transfected with 2 reporter genes (CAT, .beta.-galactosidase) using a liposome-based transfection technique, exhibited only low levels of enzymatically active proteins, but were able to degrade rapidly intracellular proteins and to process peptides efficiently. Chloramphenicol acetyltransferase as well as tyrosinase mRNA were detectable after transfection by reverse transcriptase-PCR, and enzyme activities became measurable. Furthermore, DC transfected with the tyrosinase gene were able to induce specific T cell activation in vitro, indicating appropriate peptide processing and presentation in DC after transfection. These data suggest new approaches to future tumor vaccination strategies.

L13 ANSWER 28 OF 53 CAPLUS COPYRIGHT 2002 ACS DUPLICATE 15  
ACCESSION NUMBER: 1995:718947 CAPLUS  
DOCUMENT NUMBER: 123:141663  
TITLE: Shigella infection induces cellular activation of T and B cells and distinct species-related changes in peripheral blood lymphocyte subsets during the course of the disease  
AUTHOR(S): Islam, Dilara; Bardhan, Pradeep Kumar; Lindberg, Alf A.; Christensson, Birger  
CORPORATE SOURCE: Dep. Immunol., Huddinge Univ. Hosp., Huddinge, Swed.  
SOURCE: Infect. Immun. (1995), 63(8), 2941-9  
CODEN: INFIBR; ISSN: 0019-9567  
DOCUMENT TYPE: Journal  
LANGUAGE: English

AB Immunophenotypic changes in peripheral blood lymphocytes (T, B, and NK cells) in patients during shigellosis was characterized by using triple-color flow cytometry. Eleven *Shigella dysenteriae* 1-infected adult patients (SDIP), 11 *Shigella flexneri*-infected adult patients (SFIP), 15 age- and sex-matched healthy controls from Bangladesh (C-B), and 15 healthy volunteers from Sweden (V-S) were studied. In SDIP and SFIP, a significant increase in the CD45RO+ cells in both CD4+ and CD8+ T cells was seen. We found evidence for sequential T-cell activation, as shown by increased proportions of CD25 and CD4+ cells; HLA-DR and CD38 on CD8+ cells, and CD54 on CD4+ and CD8+ cells. We found differences in the lymphocyte activation and subset patterns related to the infecting *Shigella* species. Thus, a decrease in CD45 expression was seen in SFIP; this decrease progressed further during the disease. The proportions of NK cells (CD56+ cells) and CD3- CD8+ cells out of the total CD8+ cells were increased in SFIP but not in SDIP. The CD3+ CD8+ CD57+ T-cell subset was significantly lower in SDIP than in C-B. The proportion of B-lymphocyte-expressing activation markers CD80 and CD23 was higher in patients than in C-B. There was a significant increase in the proportion of CD4+ T cells and a significant decrease in the percentages of total B cells, the CD3+ CD8+ CD57+ T-cell subset, and the CD56+ CD16+ NK-cell subset for V-S compared with C-B. Our results indicate that distinct subset changes and activation patterns are elicited in SDIP compared with SFIP and also that the degree of activation is related to disease severity. In addn., a common sequence of cell activation was seen during the disease course. The difference in the subset patterns seen in C-B and V-S may be related to differences in the levels or spectra of infectious agents in the environment.

L13 ANSWER 29 OF 53 CAPLUS COPYRIGHT 2002 ACS DUPLICATE 16  
ACCESSION NUMBER: 1995:840524 CAPLUS  
DOCUMENT NUMBER: 123:254200  
TITLE: Interleukin-10 differentially regulates B7-

AUTHOR(S) : 1 (CD80) and B7-2 (CD86) expression  
on human peripheral blood dendritic cells  
Buelens, Christel; Willems, Fabienne; Delvaux, Anne;  
Pierard, Geraldine; Delville, Jean-Pierre; Velu,  
Thierry; Goldman, Michael

CORPORATE SOURCE: Hop. Erasme, Univ. Libre Bruxelles, Brussels, Belg.

SOURCE: Eur. J. Immunol. (1995), 25(9), 2668-72

DOCUMENT TYPE: CODEN: EJIMAF; ISSN: 0014-2980  
Journal

LANGUAGE: English

AB Most of the immunosuppressive effects of interleukin-10 (IL-10) are related to functional inhibition of antigen-presenting cells (APC). Herein, the authors investigate the influence of recombinant ( $\alpha$ )IL-10 on human dendritic cells (DC) purified from peripheral blood of healthy volunteers. First, the authors found that rIL-10 inhibited in a dose-dependent manner the proliferative responses as well as the prodn. of IL-2 and interferon-gamma. (IFN-gamma.) in mixed lymphocyte reaction (MLR) between purified T cells and DC. This rIL-10 effect could be attributed to a direct effect on DC, as DC preincubated with rIL-10 were deficient in the induction of alloreactive T cells even when anti-IL-10 neutralizing mAb was added at the time of MLR. Flow cytometric anal. indicated that rIL-10 did not modify the expression of ICAM-1 (CD54) and B7-1 (CD80), but decreased HLA-DR and B7-2 (CD86) expression at the DC surface. The authors conclude that the inhibitory effect of rIL-10 on primary alloreactive T cell responses involves down-regulation of class II MHC and B7-2 expression at the DC surface.

L13 ANSWER 30 OF 53 CAPLUS COPYRIGHT 2002 ACS DUPLICATE 17  
ACCESSION NUMBER: 1995:840493 CAPLUS  
DOCUMENT NUMBER: 123:254196  
TITLE: Differential effects of interleukin-10 on the expression of HLA class II and CD1 molecules induced by granulocyte/macrophage colony-stimulating factor/interleukin-4

AUTHOR(S) : Thomassen, Henrike; Kahan, Melvyn; Londei, Marco  
CORPORATE SOURCE: Kennedy Inst. Rheumatol., London, W6 8LW, UK  
SOURCE: Eur. J. Immunol. (1995), 25(9), 2465-70  
CODEN: EJIMAF; ISSN: 0014-2980  
DOCUMENT TYPE: Journal  
LANGUAGE: English

AB Interleukin (IL)-10 down-regulates HLA class II mol., whether constitutively expressed or up-regulated by interferon-gamma. or IL-4 on monocytes but not on B lymphocytes. In this study the authors show that IL-10 does not inhibit HLA class II expression induced by the combination granulocyte/macrophage colony-stimulating factor and IL-4 on monocytes, although it simultaneously abrogates the expression of CD1 mol. induced by the same combination of cytokines. CD1 mol. can act as element of genetic restriction for CD4+ CD8-T lymphocytes, and the suppression of CD1 expression by IL-10 abolished antigen presentation to CD1-restricted CD4+ CD8-T cell receptor-pos. T cells. Although HLA class II expression was not down-regulated by IL-10, the antigen specific proliferative response of CD4+ T cells was nevertheless decreased. This was not caused by down-regulation of known co-stimulatory mol. such as B7.1, B7.2 and ICAM-1. IL-10 decreased the antigen specific proliferative response further by directly influencing the T lymphocytes. The results indicate that IL-10 exerts some of its immunoregulatory functions by differential modulation of antigen presenting mol., induced by the same combination of cytokines.

L13 ANSWER 31 OF 53 CAPLUS COPYRIGHT 2002 ACS DUPLICATE 18  
ACCESSION NUMBER: 1995:766933 CAPLUS  
DOCUMENT NUMBER: 123:167576  
TITLE: Establishment of a cell line with features of early dendritic cell precursors from fetal mouse skin

AUTHOR(S) : Girolomoni, Giampiero; Lutz, Manfred B.; Pastore, Saveria; Assmann, Caroline U.; Cavani, Andrea; Ricciardi-Castagnoli, Paola

CORPORATE SOURCE: Lab. of Immunology, Inst. Dermopatico dell'Immacolata, Rome, Italy  
SOURCE: Eur. J. Immunol. (1995), 25(8), 2163-9  
CODEN: EJIMAF; ISSN: 0014-2980  
DOCUMENT TYPE: Journal  
LANGUAGE: English

AB During ontogeny, the skin is progressively populated by major histocompatibility complex class II-neg. dendritic cell (DC) precursors that then mature into efficient antigen-presenting cells (APC). To characterize these DC progenitors better, we generated myeloid cell lines from fetal mouse skin by infecting cell suspensions with a retroviral vector carrying an envAKR-mycM2 fusion gene. These cells, represented by the line FSDC, displayed a dendritic morphol. and their proliferation in serum-free medium was promoted by granulocyte/macrophage colony-stimulating factor (GM-CSF), but not by macrophage-CSF. FSDC expressed strong surface-membrane ATP/ADPase activity, intracellular staining for 2A1 antigen, and a surface phenotype consistent with a myeloid precursor: H-2d, b+, I-Ad, b+, CD54+, CD11b+, CD11c+, 2.4G2+, F4/80+, CD44+, 2F8+, ER-MP 12-, Sca-1+, Sca-2+, NLDC-145-, B7.2+, B7.1+, J11d-, B220-, Thy-1-, and CD3-. FSDC stimulated poorly allogeneic or syngeneic T cells in the primary mixed-leukocyte reaction, and markedly increased this function after treatment with GM-CSF, GM-CSF and interleukin (IL)-4 or interferon-gamma. (IFN-gamma.); in contrast, stem cell factor, IL-1.alpha. and tumor necrosis factor-alpha. had no effect. Preculture with IFN-gamma. was required for presentation of haptens to primed T cells in vitro. However, FSDC, even after cytokine activation, were less potent APC than adult epidermal Langerhans cells in both of the above assays. Finally, FSDC derivatized with haptens and injected either i.v. or s.c. could efficiently induce contact sensitivity responses in naive syngeneic mice. The results indicate that fetal mouse skin is colonized by myeloid precursors possessing a macrophage/immature DC-like surface phenotype and priming capacity in vivo. These cells need further differentiation and activation signals (e.g. cytokines) to express their antigen presenting potential in vitro.

L13 ANSWER 32 OF 53 CAPLUS COPYRIGHT 2002 ACS DUPLICATE 19  
ACCESSION NUMBER: 1995:692473 CAPLUS  
DOCUMENT NUMBER: 123:109667  
TITLE: Mechanism of enhanced antigen presentation by B cells activated with anti-mu plus interferon-gamma.: role of B7-2 in the activation of naive and memory CD4+ T cells

AUTHOR(S) : Morokata, Tatsuaki; Kato, Takuma; Igarashi, Osamu; Nariuchi, Hideo

CORPORATE SOURCE: The Institute of Medical Science, The University of Tokyo, Tokyo, 108, Japan  
SOURCE: Eur. J. Immunol. (1995), 25(7), 1992-8  
CODEN: EJIMAP; ISSN: 0014-2980  
DOCUMENT TYPE: Journal  
LANGUAGE: English  
AB B cells activated with anti-.mu. antibody plus interferon (IFN)-gamma exerted strong antigen presenting activity for T cell proliferation. The enhanced antigen presentation function was shown to be due to the increase in B7-2 expression. When B cells were stimulated with anti-.mu., expression of MHC major histocompatibility complex class II, heat-stable antigen (HSA), ICAM-1, and B7-2 was increased. The presence of IFN-gamma further augmented the expression of B7-2 on anti-.mu.-stimulated B cells. B7-1 was not expressed on B cells under these conditions. The participation of B7-2 in the elicitation of the proliferative response of T cells was confirmed by the inclusion of anti-B7-2 antibody in cultures. The enhanced expression of either HSA or ICAM-1 was shown not to play a major role in the increased B cell antigen presentation capacity. The major T cell population responding to this activated B cell antigen presentation was shown to be CD44low naive CD4+ T cells, whereas CD45RBlow memory CD4+ T cells responded only weakly. The difference in proliferative responses between naive and memory CD4+ T cells was explained by the different efficiency in IL-2 prodn. of these cell populations in response to antigen presentation by B cells activated by anti-.mu. plus IFN-gamma. Thus, IFN-gamma plays an important role in recruitment of naive T cells for an immune response.

L13 ANSWER 33 OF 53 CAPLUS COPYRIGHT 2002 ACS DUPLICATE 20  
ACCESSION NUMBER: 1996:122224 CAPLUS  
DOCUMENT NUMBER: 124:200004  
TITLE: Bone marrow-derived dendritic cell progenitors (NLDC 145+, MHC class II+, B7-1dim, B7-2-) induce alloantigen-specific hyporesponsiveness in murine T lymphocytes  
AUTHOR(S): Lu, Lina; McCaslin, Delbert; Starzl, Thomas E.; Thomson, Angus W.  
CORPORATE SOURCE: Pittsburgh Transplantation Institute, University Pittsburgh, Pittsburgh, PA, 15213, USA  
SOURCE: Transplantation (1995), 60(12), 1539-45  
CODEN: TRPLAU; ISSN: 0041-1337  
DOCUMENT TYPE: Journal  
LANGUAGE: English  
AB The functional maturation of dendritic cells (DC) and other antigen-presenting cells is believed to reflect the upregulation of cell surface major histocompatibility complex (MHC) class II and other T cell costimulatory mol., esp. the CD28 ligands B7-1 (CD80) and B7-2 (CD86). In this study, we propagated cells exhibiting characteristics of DC precursors from the bone marrow (BM) of B10 mice (H-2b; I-A+) in response to granulocyte-macrophage colony stimulating factor (GM-CSF). The methods used were similar to those employed previously to propagate DC progenitors from normal mouse liver. Cells expressing DC lineage markers (NLDC 145+, 33D1+, N418+) harvested from 8-10-day GM-CSF stimulated BM cell cultures were CD45+, heat-stable antigen+, CD54+, CD44+, MHC class II+, B7-1dim but B7-2- (costimulatory mol.-deficient). Supplementation of cultures with interleukin-4 (IL-4) in addn. to GM-CSF however, resulted in marked upregulation of MHC class II and B7-2 expression. These latter cells exhibited potent allostimulation activity in primary mixed leukocyte cultures. In contrast, the cells stimulated with GM-CSF alone were relatively weak stimulators and induced alloantigen-specific hyporesponsiveness in allogeneic T cells (C3H; H-2k; I-E+) detected upon restimulation in secondary MLR. This was assocd. with blockade of IL-2 prodn. Reactivity to third-party stimulators was intact. The hyporesponsiveness induced by the GM-CSF stimulated, costimulatory mol.-deficient cells was prevented by incorporation of anti-CD28 monoclonal antibody in the primary MLR and was reversed by addn. of IL-2 to restimulated T cells. The findings show that MHC class II+ B7-2- cells with a DC precursor phenotype can induce alloantigen-specific hyporesponsiveness in vitro. Under the appropriate conditions, such costimulatory mol.-deficient cells could contribute to the induction of donor-specific unresponsiveness in vivo.

L13 ANSWER 34 OF 53 CAPLUS COPYRIGHT 2002 ACS DUPLICATE 21  
ACCESSION NUMBER: 1995:820330 CAPLUS  
DOCUMENT NUMBER: 123:225399  
TITLE: The primary alloresponse of human CD4+ T cells is dependent on B7 (CD80), augmented by CD58, but relatively uninfluenced by CD54 expression  
AUTHOR(S): Hargreaves, Roseanna; Logiou, Vassiliki; Lechner, Robert  
CORPORATE SOURCE: Department of Immunology, Royal Postgraduate Medical School, London, W12 0NN, UK  
SOURCE: Int. Immunol. (1995), 7(9), 1505-13  
CODEN: INIMEN; ISSN: 0953-8178  
DOCUMENT TYPE: Journal  
LANGUAGE: English  
AB Conflicting data have been reported regarding the relative abilities of B7, ICAM-1 and LFA-3 to provide co-stimulation for the induction of a primary T cell alloproliferative response. A series of naturally HLA-DR-expressing cell lines and panels of human and murine transfectants expressing DR alloantigens in conjunction with combinations of mouse or human B7-1, human LFA-3 and human ICAM-1 were used to analyze the contributions of these mol. to primary alloproliferative responses by adult and cord blood CD4+ T cells. The results demonstrated that B7 expression is required, and may be sufficient for the induction of a primary alloresponse. The allostimulation obsd. in response to DR-expressing murine DAP.3 cells, that constitutively express B7-1, was inhibited by the presence of the murine cytolytic T lymphocyte-assocd. antigen 4-human Fc-gamma.1 fusion protein, suggesting that mouse B7-1 provides sufficient co-stimulation for a primary human alloproliferative response. Expression of supranormal levels of human B7-1 on the allostimulator cells led to a redn. in the proliferative response, suggesting that an optimal level of B7 exists which, if exceeded, leads to inhibition. Co-expression of LFA-3 with B7-1 by the allostimulator cells caused a marked increase in the proliferative response. Expression of ICAM-1 had relatively little effect. No differences were seen in the co-stimulatory requirements of naive cord blood vs. CD45R0 adult T cells. These results highlight the key mol. interactions that govern immunogenicity with relevance to inhibiting unwanted immune responses to

transplanted tissues and providing anti-tumor immunity.

L13 ANSWER 35 OF 53 CAPLUS COPYRIGHT 2002 ACS DUPLICATE 22  
ACCESSION NUMBER: 1995:744646 CAPLUS  
DOCUMENT NUMBER: 123:138647  
TITLE: Human immature thymocytes as target cells of the leukemogenic activity of human T-cell leukemia virus type I  
AUTHOR(S): Maguer-Satta, Veronique; Gazzolo, Louis; Duc Dodon, Madeleine  
CORPORATE SOURCE: Immuno-Virologie Moleculaire et Cellulaire, Centre National Recherche Scientifique, Universite Claude Bernard, Lyon, Fr.  
SOURCE: Blood (1995), 86(4), 1444-52  
DOCUMENT TYPE: CODEN: BLOOAW; ISSN: 0006-4971  
LANGUAGE: Journal English  
AB The risk of developing adult T-cell leukemia (ATL) assocd. with neonatal infection by human T-cell leukemia virus type I (HTLV-I) suggests that early events triggered by HTLV-I might be of crucial importance in initiating the multistep lymphoproliferative process leading several decades later to the development of leukemic disease. Thus, infection of thymocytes early in life might be directly correlated with the development of ATL. In the present study, we show that *in vitro* infection of mature (CD2+CD3+ or immature (CD2+CD3-) thymocytes resulted in the exogenous interleukin (IL)-2-dependent proliferation of HTLV-I-pos. thymocytes, most of them displaying a CD2+CD31-CD4+ pheno-type and expressing the CD25 mol., the alpha. chain of the IL-2 receptor. Furthermore, the CD80 and CD54 antigens, normally expressed by thymic stromal cells, were detected on these transformed thymocytes, indicating that HTLV-I-infection may disturb the cooperation between thymocytes and their thymic environment. These HTLV-I-pos. thymocytes were producing significant amt. of IL-6, which was found to be implicated in their proliferation and in the expression of CD25, as demonstrated by blocking expts. using monoclonal antibody to IL-6. The present study suggests that immature thymocytes may provide an environment favorable to the unfolding of events leading to leukemia.

L13 ANSWER 36 OF 53 CAPLUS COPYRIGHT 2002 ACS DUPLICATE 23  
ACCESSION NUMBER: 1995:757338 CAPLUS  
DOCUMENT NUMBER: 123:225838  
TITLE: CD86 (B70/B7-2) on endothelial cells co-stimulates allogeneic CD4+ T cells  
AUTHOR(S): Seino, Kenichiro; Azuma, Miyuki; Bashuda, Hisashi; Fukao, Katashi; Yagita, Hideo; Okumura, Ko  
CORPORATE SOURCE: Dep. Immunol., Juntendo Univ. Sch. Med., Bunkyo, 113, Japan  
SOURCE: Int. Immunol. (1995), 7(8), 1331-7  
DOCUMENT TYPE: CODEN: INIMEN; ISSN: 0953-8178  
LANGUAGE: Journal English  
AB In vascularized organ transplantation, vascular endothelial cells (EC) confronting recipient T cells are potentially significant APC initiating cellular immune responses that lead to rejection. In the present study, we studied the ability of human EC to stimulate allogeneic T cells and the co-stimulatory mol. involved in this response. On both human umbilical vein endothelial cells (HUVEC) and microvascular endothelial cells (MVEC), MHC class I, intercellular adhesion mol. (ICAM)-1 and CD86 were constitutively expressed as assessed by flow cytometry. After IFN-gamma. treatment, MHC class II expression was induced, and MHC class I and ICAM-1 were up-regulated. In contrast, the expression of CD86 was unchanged and CD80 was undetectable even after IFN-gamma. treatment. Highly purified CD4+ T cells proliferated in response to IFN-gamma.-treated allogeneic HUVEC and MVEC, and this response was efficiently blocked by mAb to MHC class II, ICAM-1 and CD86. Furthermore, the addn. of anti-CD86 mAb to the primary culture with allogeneic EC resulted in the induction of alloantigen-specific anergy. These results suggest that CD86 expressed on EC plays a crit. role in initiating cellular immune responses to vascularized allografts and would be an important target for immune intervention.

L13 ANSWER 37 OF 53 CAPLUS COPYRIGHT 2002 ACS  
ACCESSION NUMBER: 1995:609275 CAPLUS  
DOCUMENT NUMBER: 123:30892  
TITLE: Abnormalities of B cells and dendritic cells in SAMP1 mice  
AUTHOR(S): Haruna, Hiroki; Inaba, Mueno; Inaba, Kayo; Taketani, Shigeru; Sugiyama, Kikuya; Fukuba, Yoh; Doi, Hiroshi; Toki, Junko; Tokunaga, Rikio; Ichihara, Susumu  
CORPORATE SOURCE: First Department of Pathology, Kansai Medical University, Osaka, 570, Japan  
SOURCE: Eur. J. Immunol. (1995), 25(5), 1319-25  
DOCUMENT TYPE: CODEN: EJIMAF; ISSN: 0014-2980  
LANGUAGE: Journal English  
AB The age-related changes in the function of antigen-presenting cells (APC) were examd. using a substrain of senescence-accelerated mouse (SAMP1). In the primary mixed lymphocyte reaction (MLR), dendritic cells (DC) from aged SAMP1 mice showed less stimulatory activity than those of age-matched BALB/c or young SAMP1 mice. In the secondary MLR, the stimulatory activity of B cells was lower in aged SAMP1 mice but not in age-matched BALB/c or young SAMP1 mice. In addn., these age-related decreases in the stimulatory activity of APC were related to changes in the surface d. of major histocompatibility complex class II and intercellular adhesion mol.-1 (ICAM-1) (but not B7-1 or B7-2 mol.) on APC (DC and B cells).

L13 ANSWER 38 OF 53 CAPLUS COPYRIGHT 2002 ACS DUPLICATE 24  
ACCESSION NUMBER: 1995:609251 CAPLUS  
DOCUMENT NUMBER: 123:31143  
TITLE: Co-expression of B7-1 and ICAM-1 on tumors is required for rejection and the establishment of a memory response  
AUTHOR(S): Cavallo, Federica; Martin-Foncada, Alfonso; Bellone, Matteo; Heltai, Silvia; Gatti, Evelina; Tornaghi, Paola; Freschi, Massimo; Forni, Guido; Dellabona, Paolo; Casorati, Giulia  
CORPORATE SOURCE: CNR Immunogenetica e Oncologia Sperimentale, Universita di Torino, Italy  
SOURCE: Eur. J. Immunol. (1995), 25(5), 1154-62  
DOCUMENT TYPE: CODEN: EJIMAF; ISSN: 0014-2980  
LANGUAGE: Journal

LANGUAGE: English

AB Although the transfection of B7-1 cDNA into a few mouse tumor cell lines can induce anti-tumor T cell immunity, its expression alone is ineffective in many other tumor cell lines tested. We were interested to study what factors limit B7-1 co-stimulatory activity, and decided to investigate whether B7-1 requires the cooperation of ICAM-1 to provide the minimal co-stimulatory signal for establishing an efficient anti-tumor immunity. We show that the transfection of B7-1 cDNA into three ICAM-1+ (plasmacytoma J558L, T lymphomas EL-4 and RMA), but not into two ICAM-1- tumor cell lines (adenocarcinoma TS/A and melanoma B16.F1), is sufficient to induce their complete rejection in syngeneic mice. The expression of ICAM-1 is necessary for the rejection of the B7 expressing tumors, since the primary response elicited by B7-1+ EL-4 and RMA clones expressing reduced levels of ICAM-1 is severely reduced. Furthermore, super-transfection of ICAM-1 cDNA into B7-1+ adenocarcinoma and melanoma clones optimizes their primary rejection. Histol. examn. of transfected tumors reveals that B7-1 and ICAM-1 exert a potent pro-inflammatory activity. The intra-tumor infiltration is composed of both eosinophils and lymphomonocytes, and is already massive 5 days after the tumor challenge. The primary rejection of the B7-1+ ICAM-1+ tumors depends critically on CD8+ T cells, natural killer cells and granulocytes, but is independent of CD4+ T cells. Remarkably, in addn. to its effects on the early phases of the immune response, the co-expression of ICAM-1 and B7-1 on tumors is also necessary for the efficient induction of a memory response. In fact, only the primary challenge with B7-1+, ICAM-1+ tumor cells protects the majority of the mice from a second injection of parental tumor cells. Collectively, our findings indicate that B7-1 and ICAM-1 are fundamental components for triggering the primary injection of tumors and establishing a protective memory response. These findings may help to define new strategies for the rational application of co-stimulation in tumor immunotherapy.

L13 ANSWER 39 OF 53 CAPLUS COPYRIGHT 2002 ACS DUPLICATE 25

ACCESSION NUMBER: 1995:682349 CAPLUS  
DOCUMENT NUMBER: 123:81465

TITLE: Rapid development of murine AIDS is dependent on signals provided by CD54 and CD11a  
AUTHOR(S): Makino, Masahiko; Yoshimatsu, Kazuhiko; Azuma, Miyuki; Okada, Yoshiaki; Hitoshi, Yasumichi; Yagita, Hideo; Takatsu, Kiyoshi; Komuro, Katsutoshi  
CORPORATE SOURCE: Dep. Bact. Blood Prod., Natl. Inst. Health Japan, Tokyo, Japan  
SOURCE: J. Immunol. (1995), 155(2), 974-81  
DOCUMENT TYPE: Journal  
LANGUAGE: English

AB Murine AIDS (MAIDS) is induced by infection with the replication-defective virus (BM5def) component in the LP-BM5 murine leukemia virus (MuLV) mixt. The disease is characterized by polyclonally activated CD4+ T cells and B cells. It is known that BM5def is expressed at highest levels in B lymphocytes and that B cells serve as viral antigen-presenting cells. Full and sustained activation of CD4+ T cells against a conventional antigen (Ag) usually requires both TCR and costimulating signals. Among various mol. known to provide costimulatory function, the expression of CD54 (ICAM-1) and CD11a/CD18 (LFA-1) on MAIDS B cells was increased, whereas that of CD2, heat-stable Ag (CD24), CD80 (B7-1), and CD86 (B7-2) was unchanged from normal. C57BL/6 mice depleted of both CD54 and CD11a expression as a result of chronic administration of mAb developed no MAIDS at 4 wk and 8 wk after LP-BM5 MuLV infection. In addn., the proliferative response of B cells to mitogen was well conserved, whereas MAIDS-assocd. increases in serum Ig levels were inhibited. Replication of BM5def was suppressed markedly in infected mice treated with the CD54 and CD11a mAbs. Thus, the CD54/CD11a signal transduction pathway is a crit. determinant of MAIDS development, and the lack of an immune response against viral Ag is enough to suppress BM5def replication and to prevent MAIDS.

L13 ANSWER 40 OF 53 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1996:15333 CAPLUS  
DOCUMENT NUMBER: 124:114638

TITLE: Costimulatory molecules-mediated immuno-gene therapy  
AUTHOR(S): Hirano, Naoto  
CORPORATE SOURCE: Fac. Med., Univ. Tokyo, Tokyo, 113, Japan  
SOURCE: Igaku no Ayumi (1995), 175(9), 694-7  
DOCUMENT TYPE: Journal; General Review  
LANGUAGE: Japanese

AB A review, with 10 refs., on the importance of costimulatory factors in immune reactions of T cells relating antigen presentation-major histocompatibility antigen complex (MHC) system, tumor rejection by expression of exogenous B7 mol. in tumor cells lacking B7 expression, perspective of tumor gene therapy with B7 gene, and a putative 3rd factor in the immune reaction. Expression of class I and class II MHC mol. and costimulatory factors of B7.1, B7.2, and ICAM-1 are listed for several human leukemia cells.

L13 ANSWER 41 OF 53 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.DUPLICATE 26

ACCESSION NUMBER: 95366159 EMBASE

DOCUMENT NUMBER: 1995366159

TITLE: Dendritic antigen-presenting cells from the peripheral blood of renal-cell-carcinoma patients.  
AUTHOR: Radmayr C.; Bock G.; Hobisch A.; Klocker H.; Bartsch G.; Thurnher M.  
CORPORATE SOURCE: Department of Urology, University of Innsbruck, Anichstrasse 35, 6020 Innsbruck, Austria  
SOURCE: International Journal of Cancer, (1995) 63/5 (627-632).

ISSN: 0020-7136 CODEN: IJCNW

COUNTRY: United States

DOCUMENT TYPE: Journal; Article

FILE SEGMENT: 016 Cancer

025 Hematology

026 Immunology, Serology and Transplantation

028 Urology and Nephrology

LANGUAGE: English

SUMMARY LANGUAGE: English

AB Dendritic cells are considered to be the initiators of immune responses,

including those directed against tumors. Clinical research on dendritic cells was long hampered by the limited availability of these cells. The recent identification of cytokine combinations that mobilize dendritic cells with potent antigen-presenting cell function from peripheral blood represented a major progress. We show in this study that substantial numbers of dendritic cells can be obtained from the peripheral blood of patients with renal-cell carcinoma. The procedure requires a relatively small blood sample (40 ml) and avoids both priming of the patient with granulocyte-colony stimulating factor and leukapheresis. Approximately 2 to 8 million cells with the characteristics of dendritic cells could be obtained: phase-contrast microscopy revealed the typical cytoplasmic processes or veils; phenotypic analysis confirmed expression of dendritic-cell-associated molecules, including MHC class II, CD1a, CD4, ICAM-1 (CD54), LFA-3 (CD58), B7-1 (CD80) and B7-2 (CD86), and absence of T-cell, B-cell and monocyte markers; in addition, these cells rapidly attached to and migrated on collagen-type-I coated surfaces. Interestingly, attachment was accompanied by acquisition of the CD14 antigen; functionally, cultured dendritic cells proved to be very potent co-stimulators of the phytohemagglutinin-induced proliferation of autologous tumor-infiltrating lymphocytes. The reproducible growth of functional dendritic cells from cancer patients is encouraging for the design of immunotherapy protocols.

L13 ANSWER 42 OF 53 CAPLUS COPYRIGHT 2002 ACS DUPLICATE 27

ACCESSION NUMBER: 1995:941701 CAPLUS  
DOCUMENT NUMBER: 124:27875

TITLE: Antigen-specific B cells present cartilage proteoglycan (aggrecan) to an autoreactive T cell hybridoma derived from a mouse with proteoglycan-induced arthritis

AUTHOR(S): Brennan, F. R.; Mikecz, K.; Buzas, E. I.; Ragasa, D.; Cs-Szabo, G.; Negriou, G.; Glant, T. T.  
CORPORATE SOURCE: Rush-Presbyterian-St. Luke's Medical Centre, Rush Medical University, Chicago, IL, 60612, USA  
SOURCE: Clin. Exp. Immunol. (1995), 101(3), 414-21  
CODEN: CEXIAL; ISSN: 0009-9104

DOCUMENT TYPE: Journal  
LANGUAGE: English

AB Cartilage proteoglycan (aggrecan)-induced polyarthritis in BALB/c mice is characterized by chronic inflammation and destruction of joint tissues similar to that observed in human rheumatoid arthritis. The immunization of mice with fetal human proteoglycan (PG) elicits specific antibodies to the immunizing antigen of which a population cross-reacts with native mouse PG. This (auto)antibody production is immediately followed by an explosive proliferation of autoreactive T cells, suggesting that PG-specific B cells may participate in antigen presentation of PG to autoreactive T cells. The authors therefore isolated B cells from the spleens and lymph nodes of PG-immunized mice and examined their ability to present PG to a PG-specific T cell hybridoma. The antigen-specific T cell responses elicited by B cells from PG-immunized mice (both arthritic and clinically asymptomatic) were markedly higher than those of non-immune mice and keyhole limpet hemocyanin (KLH)-immunized mice, and these B cells could present low PG concentrations. Levels of B cell presentation corresponded with the serum levels of PG-specific antibodies, implying that these B cells were presenting the PG specifically via their surface Ig. This B cell-T cell interaction was strongly dependent on MHC class II/T cell receptor (TCR), LFA-1/intercellular adhesion mol.-1 (ICAM-1) and CD28/B7 interactions, as antibodies to Igα, ICAM-1 and B7-2 (but not to B7-1) markedly reduced presentation. These data indicate that PG-specific B cells may play an essential role in governing the development of PG-induced arthritis.

L13 ANSWER 43 OF 53 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1995:708247 CAPLUS  
DOCUMENT NUMBER: 123:109557

TITLE: Adhesion molecules in immune tolerance

AUTHOR(S): Bashuda, Hisashi  
CORPORATE SOURCE: Sch. Med., Juntendo Univ., Tokyo, 113, Japan  
SOURCE: Ensho to Men'eki (1995), 3(4), 355-60  
CODEN: ENMERA; ISSN: 0918-8371

DOCUMENT TYPE: Journal; General Review  
LANGUAGE: Japanese

AB A review, with 15 refs., on the adhesion molecules as costimulatory signal transduction molecules on antigen presenting cells (APC), and results of prolongation of graft survival by blocking of the function of adhesion molecules (LFA-1/ICAM-1 system CD28, CTLA-4/CD80 and CD88 system, CD2/CD48 system, CD2/CD48 system, and VLA-4/VCAM-1 system). The mechanisms of rejection suppression are discussed.

L13 ANSWER 44 OF 53 CAPLUS COPYRIGHT 2002 ACS DUPLICATE 28

ACCESSION NUMBER: 1995:407851 CAPLUS  
DOCUMENT NUMBER: 122:158092

TITLE: CD28 functions as an adhesion molecule and is involved in the regulation of human IgE synthesis

AUTHOR(S): Lile, Paul; Aubry, Jean-Pierre; Estroppey, Sandrine; Schnuriger, Valerie; Bonnefond, Jean-Yves  
CORPORATE SOURCE: Glaxo Inst. Molecular Biol., Geneva, Switz.  
SOURCE: Eur. J. Immunol. (1995), 25(2), 333-9  
CODEN: EJIMAF; ISSN: 0014-2980

DOCUMENT TYPE: Journal  
LANGUAGE: English

AB Activated T cells induce IgE switching in B cells via a combination of lymphokines and direct T:B cell contact. As CD28-deficient mice have reduced basal levels of IgG1 and IgG2a and diminished Ig class switching, the authors investigated whether the CD28/B7-1 (CD80) ligand pairing might also be involved in human IgE regulation. Co-incubation of an allergen-specific, human T cell clone with tonsillar B cells caused a marked up-regulation of CD28 expression, whereas, in contrast, CD45RB expression was unaffected. To test whether blocking the CD28:B7-1 interaction affected IgE synthesis, a dialyzed anti-CD28 monoclonal antibody (mAb) was added to cultures containing tonsillar B cells, pre-activated T cell clones, and interleukin-4. Anti-CD28 treatment caused a reproducible, dose-dependent inhibition of IgE, but not IgG synthesis that was accompanied by a visible decrease in cell aggregate formation. Conversely, an anti-B7-1 mAb had no effect in this system. The effect of blocking CD28-ligand interactions on lymphocyte adhesion was formally assessed on human T cell clones and B cell lines using dual intracellular staining and flow cytometry. Co-incubation with an anti-CD28 mAb, but not control IgG or anti-B7-1 mAb, resulted in a marked impairment of conjugate formation that correlated well with T cell surface expression of CD28. Using this system the authors found that an anti-CTLA-4 mAb but not

an anti-B7.2 mAb inhibited T:B cell conjugate formation. Lastly, in addn. to a direct effect of anti-CD28 mAb on conjugate formation, 14-day culture of T and B cells in the presence of anti-CD28 caused a marked decrease of ICAM-1 (CD54) expression on aggregated lymphocytes. In contrast, LFA-1 (CD18) expression was unaffected. Thus, the T cell co-stimulatory mol. CD28 is involved in the regulation of IgE synthesis in vitro. CD28 may act to a limited extent as an adhesion mol., though apparently not by pairing with B7.1 or B7.2. It is more likely that ligation of CD28 under certain conditions modulates the expression of other T and B cell surface mols.

L13 ANSWER 45 OF 53 CAPLUS COPYRIGHT 2002 ACS DUPLICATE 29

ACCESSION NUMBER: 1995:871237 CAPLUS

DOCUMENT NUMBER: 123:254544

TITLE: Regulation and function of adhesion molecule expression by human alveolar epithelial cells

AUTHOR(S): Cunningham, A. C.; Kirby, J. A.

CORPORATE SOURCE: Dep. Surgery, Univ. Newcastle upon Tyne, UK

SOURCE: Immunology (1995), 86(2), 279-86

CODEN: IMMUAJ; ISSN: 0019-2805

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The role of major histocompatibility complex (MHC) and adhesion mol. expression by alveolar epithelium on the modulation of immune responses in the lung is not understood. We have developed efficient methods to isolate, purify and culture human alveolar epithelial cells (type II pneumocytes) in vitro. The expression of MHC and adhesion mols. by isolated, cultured and cytokine-stimulated alveolar epithelial cells was quantified by flow cytometry, and demonstrated the presence T-cell ligands including class I MHC, HLA-DR and HLA-DP, intracellular adhesion mol.-1 (ICAM-1; CD54) and lymphocyte function-assocd. antigen (LFA-3; CD58), but not vascular cell adhesion mol.-1 (VCAM-1) (CD106) or B7 (CD80). The proinflammatory cytokine interferon-.gamma. (IFN-.gamma.) caused an up-regulation of class I MHC and ICAM-1. In contrast, tumor necrosis factor-.alpha. (TNF-.alpha.) and interleukin-1.beta. (IL-1.beta.) had little effect on the expression on these surface antigens by human alveolar epithelial cells. The functional activity of alveolar epithelial adhesion mols. was then studied by detg. their ability to bind allogeneic lymphocytes. An increase in lymphocyte adherence to monolayers of alveolar epithelial cells was obsd. following in vitro activation. However, up-regulation of alveolar epithelial counter receptors with the proinflammatory cytokine .gamma.-IFN did not enhance adhesion. The adhesive interaction between CD18 on lymphocytes and ICAM-1 on alveolar epithelial cells was demonstrated by the use of blocking antibodies specific for both ligands. Blockade of LFA-3 on alveolar monolayers also suppressed lymphocyte adherence. In conclusion, alveolar epithelial cells expressed MHC HLA-A,B,C, HLA-DR and -DP, and functional adhesion mols. including ICAM-1 and LFA-3.

L13 ANSWER 46 OF 53 CAPLUS COPYRIGHT 2002 ACS DUPLICATE 30

ACCESSION NUMBER: 1996:80071 CAPLUS

DOCUMENT NUMBER: 124:199967

TITLE: Immunogenicity and immunosensitivity of ex vivo human carcinomas: Interferon .gamma. and tumor necrosis factor .alpha. treatment of tumor cells potentiates their interaction with autologous blood lymphocytes

AUTHOR(S): Vankay, Farkas; Hising, Christina; Sjoewall, Kerstin; Larsson, Barbro; Rodriguez, Luis; Orre, Lotta; Klein, Eva

CORPORATE SOURCE: Microbiology and Tumour Biology Centre, Karolinska Institute, Stockholm, S-171 77, Swed.

SOURCE: Cancer Immunol. Immunother. (1995), 41(4), 217-26

CODEN: CIIMDN; ISSN: 0340-7004

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Human carcinoma cells vary appreciably in the expression of MHC class I, class II, ICAM-1 (CD54) and B7 (CD80) mols. Short-term in vitro exposure of ex vivo carcinoma cells to interferon .gamma. and tumor necrosis factor .alpha. elevated/induced the surface expression of MHC class I, class II and ICAM-1, but only rarely of B7. We found that cytokine treatment elevated the cytotoxic susceptibility and the stimulatory potential of ex vivo tumor cells. This was demonstrated (a) by the increased frequency and elevated level of auto-tumor lysis and (b) by induction of DNA synthesis and generation of cytotoxic lymphocytes in autologous mixed lymphocyte/tumor cell culture (MLTC). The MHC class I and ICAM-1 mols. on the tumor cells were required for interaction with the lymphocytes as indicated by the inhibitory effect of specific mAb both in the stimulation and in the cytotoxic tests. While the cytokine-induced increases in MHC and ICAM-1 on the low-expression tumors were probably important for the modification of functional interaction with the autologous lymphocytes, it is likely that alterations in other properties of tumor cells were also induced which contributed to the phenomenon. This was indicated by the results obtained with several tumors, which expressed indigenously high levels of these mols. but activated the autologous lymphocytes only after cytokine treatment. In several expts. the untreated targets that did not activate the lymphocytes were sensitive to the cytotoxicity of the effectors activated in MLTC. The results show that the afferent and efferent arms of the immune response have different requirements for functional interactions between lymphocytes and tumor cells.

L13 ANSWER 47 OF 53 CAPLUS COPYRIGHT 2002 ACS DUPLICATE 31

ACCESSION NUMBER: 1995:694498 CAPLUS

DOCUMENT NUMBER: 123:106613

TITLE: Hydrogen peroxide mediates UV-induced impairment of antigen presentation in a murine epidermal-derived dendritic cell line

AUTHOR(S): Caceres-Dittmar, Gisela; Ariizumi, Kiyoshi; Xu, Shan; Tapia, Felix J.; Bergstresser, Paul R.; Takashima, Akira

CORPORATE SOURCE: Dep. Dermatology, Univ. Texas Southwestern Med. Cent., Dallas, TX, 75235, USA

SOURCE: Photochem. Photobiol. (1995), 62(1), 176-83

CODEN: PHCBAP; ISSN: 0031-8655

DOCUMENT TYPE: Journal

LANGUAGE: English

AB UV-B (290-320 nm) radiation is known to impair the antigen-presenting cell (APC) function of Langerhans cells (LC), skin-specific members of the dendritic cell (DC) family. We sought to address mechanisms of this effect, focusing on the role played by hydrogen peroxide. For this

purpose, we used a newly established murine DC line, XS52, which resemble epidermal LC in several respects. The APC capacity of XS52 cells, using two different CD4+ T cell clones as responders, was inhibited significantly (>50%) by exposure to UV radiation (unfiltered FS20 sunlamps) at relatively small fluences (50-100 J/m<sup>2</sup>). UV radiation also inhibited growth factor-dependent proliferation of XS52 cells. Cell surface phenotype was relatively well preserved after irradn.; expression levels of B7-1 and B7-2 were reduced slightly, while other mol. (e.g. Ia, CD54, CD1a and CD18) were not affected. With respect to the role played by hydrogen peroxide, pretreatment with purified catalase (900 U/ml) prevented UV-induced inhibition of APC function. Short-term exposure to 3 mM H2O2 or tert-Bu H2O2 mimicked UV radiation by inhibiting APC function. Finally, intrinsic catalase activity was substantially lower in XS52 cells compared with PAM 212 keratinocytes. These results indicate that the generation of hydrogen peroxide alone is sufficient to produce some, but not all, of the deleterious effects of UV radiation on DC derived from the skin.

L13 ANSWER 48 OF 53 CAPLUS COPYRIGHT 2002 ACS DUPLICATE 32  
ACCESSION NUMBER: 1995:656243 CAPLUS  
DOCUMENT NUMBER: 123:54107  
TITLE: B cell superstimulatory influenza virus activates peritoneal B cells  
AUTHOR(S): Rott, Ortwin; Charreire, Jeannine; Mignon-Godefroy, Karine; Cash, Evelyne  
CORPORATE SOURCE: Cochin Hosp., Rene Descartes Univ., Paris, Fr.  
SOURCE: J. Immunol. (1995), 155(1), 134-42  
CODEN: JOIMAJ3; ISSN: 0022-1767  
DOCUMENT TYPE: Journal  
LANGUAGE: English  
AB The authors evaluated the potential of B cell "superstimulatory" influenza viruses to activate peritoneal B cells (PBC) from BALB/c mice contg. both CD5+ and CD5- "sister" cells. Like conventional B cells, PBCs responded to influenza viruses in a hemagglutinin glycoprotein (HA) subtype-specific manner with proliferation and vigorous Ig synthesis. However, a no. of HA subtypes that are highly stimulatory for conventional B cells failed to induce significant responses of PBC. Isotype-detn. revealed a high predominance of IgM and only very low prodn. of IgA and IgG. HA-activated CD5+ B cells showed a hyper-expression of various activation markers, including MHC class II, intercellular adhesion mol. 1 (CD54), and B7-1 mol. In contrast to conventional B cells, where activation by HA is antagonized by phorbol esters (PMA), HA and PMA acted synergistically on PBC, suggesting differential activation requirements of B-2 cells vs. PBC in response to HA. Like HA stimulation of B2 cells, virus-triggered proliferation of PBC was abrogated by a simultaneous treatment with F(ab')2 fragments of anti-Ig Ab and exhibited synergistic effects with LPS stimulation. HA-mediated proliferative responses of PBC, but not of B-2 cells, were pos. controlled by various cytokines, including IL-4 and IL-10, and to a lesser extent by IL-6. This data represents the first example of a stimulation of peritoneal B cells by a polyclonal-activating virus, findings that call for considering infections with polyclonal B cell-stimulatory viruses as a means of expanding the pool of potentially autoreactive CD5 B cells.

L13 ANSWER 49 OF 53 CAPLUS COPYRIGHT 2002 ACS DUPLICATE 33  
ACCESSION NUMBER: 1995:656233 CAPLUS  
DOCUMENT NUMBER: 123:81524  
TITLE: Costimulatory requirements of naive CD4+ T cells. ICAM-1 or B7-1 can costimulate naive CD4 T cell activation but both are required for optimum response  
AUTHOR(S): Dubey, Caroline; Croft, Michael; Swain, Susan L.  
CORPORATE SOURCE: Dep. Biol., Univ. California, San Diego, La Jolla, CA, 92093, USA  
SOURCE: J. Immunol. (1995), 155(1), 45-57  
CODEN: JOIMAJ3; ISSN: 0022-1767  
DOCUMENT TYPE: Journal  
LANGUAGE: English  
AB Efficient initiation of a CD4 T cell response requires both activation through the TCR and costimulation provided by mol. on APC with counterreceptors on the T cell. We investigated the relative contribution of the ICAM-1:LFA-1 and B7:CD28/CTLA-4 costimulatory pathways in naive T cell activation, using either anti-CD28 Ab or fibroblast cell lines transfected with I-Ek, which express either no costimulatory mol., ICAM-1 alone, B7-1 alone, or ICAM-1 and B7-1 together. Peptide Ag or immobilized anti-CD3 was used to provide the TCR signal. CD4 T cells from mice transgenic for the V.beta.3/V.alpha.11 TCR, which recognize a peptide of pigeon cytochrome c complexed to I-Ek, were used as a source of naive T cells. Naive T cells stimulated with Ag or anti-CD3 responded well to high nos. of APC expressing either ICAM-1 alone or B7-1 alone. However, APC expressing both ICAM-1 and B7-1 were much better stimulators of proliferation and IL-2 secretion at low cell nos., and were far superior inducers of IL-2 at higher nos., indicating a synergy between the two pathways. Stimulation provided by ICAM-1 could not be solely attributed to adhesive strengthening of other pathways, since costimulation was seen when immobilized anti-CD3 was used and when ICAM-1 only APC were added, indicating that ICAM-1 was in fact acting as a classic costimulatory mol. Both the magnitude of the response and the amt. of costimulation required for response were dependent on the intensity of TCR interaction. These results suggest that an efficient naive T cell response requires both a strong TCR signal and more than one costimulatory signal that will synergize with the TCR signal. This offers an explanation as to why APC such as dendritic cells and activated B cells, which express high levels of multiple costimulatory/adhesion mol., are the only APC that elicit naive T cell responses.

L13 ANSWER 50 OF 53 CAPLUS COPYRIGHT 2002 ACS DUPLICATE 34  
ACCESSION NUMBER: 1995:514551 CAPLUS  
DOCUMENT NUMBER: 122:312753  
TITLE: B7-1 expression decreases tumorigenicity and induces partial systemic immunity to murine neuroblastoma deficient in major histocompatibility complex and costimulatory molecules  
AUTHOR(S): Katsanis, Emmanuel; Xu, Zhiyi; Bausero, Maria A.; Dancisak, Betsy B.; Gordon, Keith B.; Davis, Geoffrey; Gray, Gary S.; Orchard, Paul J.; Blazar, Bruce R.  
CORPORATE SOURCE: Department of Pediatrics, University of Minnesota, Minneapolis, MN, USA  
SOURCE: Cancer Gene Ther. (1995), 2(1), 39-46  
CODEN: CGTHEC; ISSN: 0929-1903

DOCUMENT TYPE: Journal  
LANGUAGE: English  
AB Neuroblastoma may escape an immune attack by virtue of its low expression of surface accessory mol. essential in the antitumor response. Murine neuroblastoma, neuro-2a, was transduced with the retroviral vector LB7-1SN to examine the influence of B7-1 expression on the immune response directed against a low major histocompatibility class (MHC) I and class II neg., B7-2, and ICAM-1 neg. tumor. Using a retroperitoneal model for implantation of neuroblastoma in its natural site, the authors demonstrated that expression of B7-1 by neuro-2a reduces its tumorigenicity. Coinjection of B7-1-pos. and -neg. cells improved survival compared with mice receiving B7-1-neg. cells alone. This was dependent on the ratio of B7+ to B7-1 neuro-2a cells injected. CD8+ and not CD4+ T-cell depletion significantly increased tumor-induced mortality in syngeneic A/J mice, indicating that B7-1 decreases tumorigenicity primarily by direct costimulation of CD8+ T cells. Rejection of N-2a/B7-1 tumors or preimmunization with irradiated N-2a/B7-1 cells did not increase protection to challenge with unmodified neuro-2a cells over mice vaccinated with N-2a/neo. Furthermore, cytotoxic T lymphocyte (CTL) precursor frequencies were not significantly higher after in vivo priming and in vitro stimulation with irradiated N-2a/B7-1 compared with N-2a/neo, indicating that B7-1 costimulation by the tumor, in the absence of adequate antigen presentation by MHC mol., may limit the generation of effective CTLs.

L13 ANSWER 51 OF 53 CAPLUS COPYRIGHT 2002 ACS  
ACCESSION NUMBER: 1996:160483 CAPLUS  
DOCUMENT NUMBER: 124:254609  
TITLE: TCSA painting plus UVA irradiation augments the expression of B7-2 and MHC class II molecules on Langerhans cells.  
AUTHOR(S): Nishijima, Takafumi; Tokura, Yoshiki; Imokawa, Genji; Takigawa, Masahiro  
CORPORATE SOURCE: School Medicine, Hamamatsu University, Hamamatsu, Japan  
SOURCE: Photomed. Photobiol. (1995), 17, 29-30  
DOCUMENT TYPE: CODEN: PHPHEA; ISSN: 0912-232X  
LANGUAGE: Journal English  
AB The intensity of contact photosensitivity (CPS) reaction to 3,3'4',5-tetrachlorosalicylanilide (TCSA) is dependent on the dose of TCSA and irradiance of UV A light (UVA) in both the induction and elicitation phases. BALB/c mice were painted with 5 .mu.L of 0.1% TCSA on the earlobes and then irradiated with UVA at 16 J/cm<sup>2</sup>. Twenty four h later epidermal cells (EC) were prep'd. from these earlobes and the levels of intercellular adhesion mol. (ICAM)-1, B7-1, B7-2 and major histocompatibility complex (MHC) class II on these EC were analyzed using flow cytometry. Langerhans cells (LC) were identified with the expression of MHC class II. On LC from untreated earlobes ICAM-1 and B7-2 were weakly expressed, but B7-1 was not detected. The levels of B7-2 and I-Ad on LC were augmented by TCSA painting plus UVA irradn., while ICAM-1 and B7-1 were not changed by these treatments. Keratinocytes from untreated epidermis expressed ICAM-1 alone, which was augmented by TCSA painting plus UVA irradn. The augmentation of the expression of B7-2 and I-Ad on LC depended on both the TCSA amt. and UVA irradiance. A dot plot anal. showed that the expression of B7-2 and that of MHC class II were correlated with each other and the percentage of these highly expressing LC was increased with increasing doses of TCSA and UVA. Thus, we conclude that LC expressing high amts. of B7-2 and MHC class II play an important role in the magnitude of CPS.

L13 ANSWER 52 OF 53 CAPLUS COPYRIGHT 2002 ACS DUPLICATE 35  
ACCESSION NUMBER: 1994:455819 CAPLUS  
DOCUMENT NUMBER: 121:55819  
TITLE: Regulation of immunostimulatory function and costimulatory molecule (B7-1 and B7-2) expression on murine dendritic cells  
AUTHOR(S): Larsen, Christian P.; Ritchie, Shannon C.; Hendrix, Rose; Linsley, Peter S.; Hathcock, Karen S.; Hodes, Richard J.; Lowry, Robin P.; Pearson, Thomas C.  
CORPORATE SOURCE: Sch. Med., Emory Univ., Atlanta, GA, 30322, USA  
SOURCE: J. Immunol. (1994), 152(11), 5208-19  
DOCUMENT TYPE: CODEN: JOIMA3; ISSN: 0022-1767  
LANGUAGE: Journal English  
AB Dendritic cells (DC) play a crit. role in the initiation of T cell-mediated immune responses, and express costimulatory mol. that are required for optimal activation of unprimed T cells. Studies on the regulation of the costimulatory mol. on DC have produced evidence from several systems that GM-CSF can up-regulate expression of CTLA4 counter receptor (CTLA4-CR) (but not intercellular adhesion mol. 1 (ICAM-1) and heat stable Ag (HsAg)) on DC. This is demonstrated on splenic DC, Langerhans cells, kidney DC in culture, and in a skin-explant culture system, in which the increased expression of CTLA4-CR on Langerhans cells (LC) occurs concomitantly with their migration out of skin. Interestingly, despite the ability of both GM-CSF and IFN-.gamma. to increase CTLA4-CR and maintain similar levels of ICAM-1, HsAg, and MHC mol. expression, the functional consequences of these cytokines on splenic DC are distinctly different. GM-CSF enhances the ability of DC to stimulate both T cell proliferation and cytokine release, whereas IFN-.gamma. causes no increase in immunostimulatory function. Further anal. of the CTLA4-CR on these cell populations by using the GL-1 and IG10 mAbs has shown that GM-CSF-cultured DC express high levels of both B7-1 and B7-2, whereas IFN-.gamma.-cultured DC express increased levels of only B7-2. These results suggest that optimal stimulation of unprimed T cells to proliferate and release cytokines may require participation of both of these CTLA4 counter receptors, and confirm the importance of GM-CSF for the maturation of DC into potent stimulators of T cell activation.

L13 ANSWER 53 OF 53 CAPLUS COPYRIGHT 2002 ACS  
ACCESSION NUMBER: 1995:633482 CAPLUS  
DOCUMENT NUMBER: 123:31188  
TITLE: Analysis of adhesion molecule-mediated signal transduction between T cells  
AUTHOR(S): Wanibuchi, Masahiko; Murakami, Masaaki  
CORPORATE SOURCE: Sch. Med., Sapporo Med. Univ., Japan  
SOURCE: Sapporo Igaku Zasshi (1994), 63(5-6), 221-9

CODEN: SIZSAR; ISSN: 0036-472X

DOCUMENT TYPE: Journal  
LANGUAGE: Japanese

AB T cell activation requires engagement of the T cell receptor (TCR) with an immunogenic peptide bound to a major histocompatibility complex (MHC) mol. and a costimulatory signal provided by the antigen-presenting cell (APC). Although these events result in T cell clonal expansion, ligation of the TCR alone (lack of a costimulatory signal) does not stimulate T cell activation, but rather results in unresponsiveness known as T cell energy. Most investigations of the T cell activation mechanism have focussed on the system consisting of classical APC and T cells, but it is known that T cell can coexpress not only the adhesion mols. that provide costimulatory signals to T cells, but also their counter-receptors. In this paper, we analyze the role of adhesion mols. in T cell activation using a mouse CD4+ T cell clone, DB14. DB14 cells were able to proliferate upon stimulation of the TCR/CD3 complex alone either by appropriate MHC class II cDNA transfected CHO cells plus peptides or anti-CD3 monoclonal antibodies (mAb). Moreover the magnitude of anti-CD3 mAb-induced T cell proliferation was dependent on cell d., suggesting that cell to cell contact is important for the anti-CD3 mAb-induced DB cell proliferation. The DB14 cell expressed B7-1, CD28, ICAM-1 and LFA-1 mols. on its cell surface. Importantly, anti-CD3 mAb-induced proliferation was inhibited by CTLA-4 Ig or anti-LFA-1 mAb and the inhibitory effect of anti-LFA-1 mAb was stronger than that of CTLA-4 Ig. These results suggest that DB14 cells require two signals, the first, a TCR-mediated signal by anti-CD3 mAb and the second, a costimulatory signal through interaction of B7/CD28 and LFA-1/ICAM-1 pathways. Thus adhesion mols. on DB14 cells can provide a costimulatory signal for T cell proliferation, which suggests that T cells may provide costimulatory signals to each other at inflamed regions in vivo.

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FILE 'MEDLINE, CAPLUS, EMBASE, BIOSIS' ENTERED AT 11:53:01 ON 10 JUL 2002  
L1 14884 S WEBB S?/AU OR WINGVIST O?/AU OR KARLSSON L?/AU OR JACKSON M?/  
L2 198 S L1 AND CD4?  
L3 185 S L2 NOT CD40  
L4 13 S L3 AND (CD80 OR B7.1)  
L5 6 DUP REM L4 (7 DUPLICATES REMOVED)  
L6 5 S L5 AND (ICAM? OR CD102 OR CD50 OR CD54)  
L7 326975 S MHC OR CD4?  
L8 310771 S L7 NOT CD40  
L9 3374 S L8 AND (CD80 OR B7.1)  
L10 533 S L9 AND (ICAM? OR CD102 OR CD50 OR CD54)  
L11 2412 S L0 AND PD<19960523  
L12 108 S L10 AND PD<19960523  
L13 53 DUP REM L12 (55 DUPLICATES REMOVED)  
L14 1 S L13 AND (HLA (1N) DP)

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